WO 98/41648 PCT/US98/05419

199

232/116

The frequency of heterozygotes for the seven sequence variants ranged from 3-11% among the 36 individuals tested. Some of the sequence variances appear to occur more commonly in certain racial or ethnic groups. For example, heterozygotes for four sequence variances (at nucleotides 1059, 1428, 3324 and 3375) were detected solely or predominantly in North American Blacks, with heterozygote frequencies of 1/4 or 2/4. The nucleotide 2538 variance was detected solely in North American Whites (4/16) and results in an amino acid exchange (see below). The nucleotide 3397 sequence variance was detected solely in one Japanese individual (of four tested). The nucleotide 2538 sequence variant results in an aspartic acid vs. glutamic acid substitution at amino acid 740 of the 1024 amino acid protein. This residue lies in the cytoplasmic loop of the 1 subunit.

5

10

15

20

25

The alpha1 subunit of Sodium Potassium ATPase maps to chromosome 1p13-p11

The gene for the 1 subunit of sodium-potassium ATPase has been mapped to chromosome band 1p13-p11 by several techniques. Yang-Feng et al. (10) assigned the ATP1A1 gene to 1p21-cen by Southern analysis of DNA from panels of rodent/human somatic cell hybrid lines. This localization was confirmed and refined by Chehab et al., who showed that the gene for the ATP1A1 subunit is on 1p13-p11 using hybridization to flow-sorted chromosomes and *in situ* hybridization (9).

Chromosome band 1p13-p11 is a site of frequent loss of heterozygosity

The short arm of chromosome 1 is comparatively well investigated for allele loss, especially in breast and colon cancers, however most of these studies are principally concerned with the 1p36 region, and there is comparatively little data on 1p13-p11. The best studies of proximal 1p allele loss are in breast and testicular cancers. These studies show LOH occurs in approximately 15-35% of breast cancers (11,12) and 15-25% of testicular cancers (13). Data from more distal loci on 1p show >25% LOH in

glioma, colon cancer, stomach cancer, ovarian cancer, and liver cancer (14). The LOH observed in this region indicates that other essential genes mapping to the 1p chromosomal arm, and especially to the 1p11 region, which have LOH and for which sequence variances, and therefore heterozygotes for a sequence variance, exist in normal somatic cells of individuals in a population are potential target genes

References

5

10

20

- 1. Jorgensen, P.L. Na, K-ATPase, structure and transport mechanism. In De Pont, ed. Molecular Aspects of Transport Proteins, Elsevier Science Publishers, The Netherlands, 1992, pp. 1-26..
- 2. Sweadner, K.J. (1989) Biochimica et Biophysica Acta 1154: 185-220.
- 3. Lingrel, J.B., Orlowski, J., Shull, M.M. and E.M. Price (1989) Prog. Nucleic Acid Research and Mol. Biol. 38: 37-89.
- 4. Price, E.M. and J.B. Lingrel (1988) Structure-function relationships in the Na, K-ATPase a subunit: site directed mutagenesis of glutamine-111 to arginine and asparagine 122 to aspartic acid generates a ouabain-resistant enzyme. *Biochemistry* 27: 8400-8408.
 - 5. Emanuel, J.R., Graw, S., Housman, D. and R. Levenson (1989) Identification of a region within the Na, K-ATPase a subunit that contributes to differential ouabain sensitivity. *Molecular and Cellular Biology* 9: 3744-3749.
 - 6. Kawakami, K., Ohta, T., Nojima, H., Nagano, K. (1986) Primary structure of the alpha-subunit of human Na,K-ATPase deduced from cDNA sequence. *J. Biochem.* 100: 389-397.
- 7. Ovchinnikov, Y. A., Monastyrskaya, G. S., Broude, N. E., et al. (1987) The family of human Na+,K+-ATPase genes: a partial nucleotide sequence related to the alphasubunit. *FEBS Lett.* 213: 73-80.
 - 8. Shull, M. M. and J.B. Lingrel (1987) Multiple genes encode the human Na+,K+-ATPase catalytic subunit. *Proc. Nat. Acad. Sci. U.S.A.* 84: 4039-4043.

- 9. Chehab, F. F., Kan, Y. W., Law, M. L., Hartz, J., Kao, F.-T. and R. Blostein (1987) Human placental Na+,K+-ATPase alpha subunit: cDNA cloning, tissue expression, DNA polymorphism, and chromosomal localization. *Proc. Nat. Acad. Sci. U.S.A.* 84: 7901-7905.
- 10. Yang-Feng, T.L., Schneider, J.W., Lindgren, V., Shull, M.M., Benz, E.J., Jr., Lingrel, J.B. and U. Francke (1988) Chromosomal localization of human Na+,K+-ATPase alpha- and beta-subunit genes. *Genomics* 2: 128-138.
 - 11. Bieche, I., Champeme, M.H., Matifas, F., Cropp, C.S., Callahan, R. and R. Lidereau (1993) Two distinct regions involved in 1p deletion in human primary breast cancer. *Cancer Res.* 53:1990-4.
 - 12. Nagai H, Negrini M, Carter SL, et al. (1995) Detection and cloning of a common region of loss of heterozygosity at chromosome 1p in breast cancer. *Cancer Res.* 55:1752-7.
 - 13. Mathew S., Murty V.V., Bosl G.J., Chaganti R.S.K. (1994) Loss of heterozygosity identifies multiple sites of allelic deletions on chromosome 1 in human male germ cell tumors. *Cancer Res.* 54:6265-9.
 - 14. Yeh S.H., Chen P.J., Chen H.L., Lai M.Y., Wang C.C. and D.S. Chen (1994) Frequent genetic alterations at the distal region of chromosome 1p in human hepatocellular carcinomas. *Cancer Res.* 54:4188-92.

10

15

Example 12: Ribonucleotide Reductase, M1 subunit (RRM1) - Target Gene VARIA200

25 Ribonucleotide Reductase is essential for cell growth

Human ribonucleotide reductase (also called ribonucleoside diphosphate reductase) is essential in dividing cells for the production of deoxyribonucleotides prior to DNA synthesis in S phase. Ribonucleotide reductase catalyzes the reduction of all four

10

15

20

25

ribonucleoside diphosphates to the corresponding deoxyribonucleoside diphosphates by replacing the 2' hydroxyl moiety of ribose with a hydride ion to form deoxyribose; these reactions constitute the first committed steps in the creation of DNA precursors (deoxyribonucleotides), and are therefore tightly regulated by allosteric nucleotide binding sites on the M1 subunit (2,3). The enzyme is an 2 2 tetramer apparently conserved in all prokaryotes and eukaryotes (1). The two subunits, M1 and M2, are both required for enzyme activity. The RRM2 subunit contains the catalytic site, while the RRM1 subunit provides an indispensable allosteric function. (See pages 758-763 of Biochemistry by C.K. Mathews and K.E. van Holde, Benjamin/Cummings Publishing Biochemistry, Company, Redwood City, 1990 for a fuller account of ribonucleotide reductase function.)

Both ribonucleotide reductase subunits are expressed in all proliferating cells but are generally nondetectable in quiescent cells. Ribonucleotide reductase subunit M2 is the target of several antineoplastic compounds, including hydroxyurea. Hydroxyurea is used in the chemotherapy of a variety of myeloproliferative disorders (4). It acts by reversibly destroying a tyrosyl free radical in the catalytic site of the M2 subunit (3). Hydroxyurea and other ribonucleotide reductase poisons are specific for the S phase of the cell cycle, resulting in growth arrest at the G1-S boundary and apoptotic death in tumor cells (5). Exposure of cell cultures to hydroxyurea results in selection of cells expressing high levels ribonucleotide reductase, demonstrating that ribonucleotide reductase is required for these cells to grow (6).

The human ribonucleotide reductase gene has sequence variances

The cDNA sequence of the human ribonucleotide reductase M1 subunit has been published by two groups (7,8). We undertook a systematic search for DNA sequence variance in the cDNA of the M1 subunit by analysing 36 unrelated individuals using the single strand conformation polymorphism technique. Primers were designed using

the sequence of Parker et al. (GENBANK accession X59543; see ref. 7). SSCP analysis revealed 4 sequence variances, and subsequent DNA sequence analysis confirmed that nucleotides 1037 (C vs. A), 2410 (A vs. G), 2419 (A vs. G) and 2717 (T vs. A) vary as shown in the Target Summary Table. (The sequence variance at nt 1037 was previously noted by Parker et al., ref. 7.) Also, DNA sequencing revealed an insertion/deletion sequence variance: the 9 consecutive T nucleotides between positions 2724 and 2732 (numbering from ref. 7) were augmented in some cDNAs by a tenth T. (This sequence variance is designated T9 vs. T10 in the Target Summary Table.)

10

5

Both alleles at nt 1037 were detected in North American Whites, Hispanics, Chinese, Japanese, Arabs and Indians. Similarly, both alleles of the sequence variance at nt 2410 were detected in virtually all tested populations: North American White, North American Black, Hispanic, Chinese, Arab and Indian. In contrast, the sequence variances at nt 2419 and 2717 were prevalent in North American Blacks, Hispanics, Chinese, and Japanese, but not North American Whites. The insertion/deletion sequence variance at nt 2724 was only studied in four individuals so no firm conclusions can be drawn regarding population distribution, however it appears to be in linkage disequilibrium with the 2419 and 2724 sequence variances.

20

15

The human ribonucleotide reductase gene maps to chromosome 11p15.5

25

The gene for human ribonucleotide reductase has been mapped to band 11p15.5 by several techniques. Initially the gene was localized by Southern hybridization analysis of human X rodent somatic cell hybrids and by chromosomal *in situ* hybridization (9). Subsequently RRM1 has been placed on a yeast artificial chromosome (YAC) physical map of chromosome 11p15 (10). The precise physical localization of the RRM1 gene facilitates interpretation of LOH results at adjacent polymorphic markers (see below).

Chromosome band 11p15.5 is a site of frequent loss of heterozygosity

The short arm of chromosome 11 is the site of several tumor suppressor genes, including the WT1 gene and the Beckwith-Weidemann syndrome gene. As a result there are many studies of LOH in 11p15.5, particularly focusing on breast, cervix, kidney, liver, lung, ovarian, stomach and testicular cancers. These studies show that the 11p15.5 band of chromosome 11 is frequently reduced to one copy (11-28). For example, LOH occurs in approximately 13-33% of breast cancers (11-13), 14-42% of cervical cancers (14), 0-50% of liver cancers (16), 0-80% of lung cancers (17-19), 18-54% of ovarian cancers (20,21), 0-71% of stomach cancers (22) and 0-50% of testicular cancers (23,24). Other studies show that 11p15.5 LOH may also be frequent in bladder cancer (25), esophageal cancer (26), some leukemias (27) and sarcomas (28). Many deletions in the 11p15.5 region span relatively short chromosomal segments (2 - 10 megabases; see ref. 17).

15

20

25

10

5

References

- 1. Caras, I.W., Levinson, B.B., Fabry, M., et al. (1985) Cloned mouse ribonucleotide reductase subunit M1 cDNA reveals amino acid sequence homology with Escherichia Coli and herpesvirus ribonucleotide reductases. *J. Biol. Chem.* 260: 7015-7022.
- 2. Thelander, L., and P. Reichard, (1979) Reduction of Ribonucleotides. *Annu. Rev. Biochem.* 48:133-158.
- 3. Reichard, P. and A Ehrenberg (1983) Ribonucleotide reductase: a radical enzyme. *Science* 221: 514-9.
- 4. Donehower, R.C. (1992) An Overview of the clinical experience with hydroxyurea. Seminars in Oncology 19:11-19, 1992.
 - 5. Wright, P.S., Cross-Doersen, D., Thong, J.P., et al. (1996) A ribonucleotide reductase inhibitor, MDL 101,731, induces apoptosis and elevates TRPM-2 mRNA levels in human prostate tumor xenografts. *Experimental Cell Research* 22: 54-60.

15

25

- 6. Cocking, J.M., Tonin, P.N., Stokoe, et al. (1987) Gene for M1 subunit of ribonucleotide reductase is amplified in hydroxyurea-resistant hamster cells. *Somat. Cell. Mol. Genet.* 13:221-33.
- 7. Parker, N.J., Begley, C.G. and R.M. Fox. (1991) The Human M1 Subunit of Ribonucleotide Reductase: cDNA Sequence and Expression in Stimulated Lymphocytes. *Nucleic Acids research* 9:3741.
- 8. Pavloff, N., Rivard, D., Masson, S., Shen, S.H. and A.M. Mes-Masson. (1992) Sequence Analysis of the Large and Small Subunits of Human Ribonucleotide Reductase. *DNA Sequence* 2:227.
- 9. Brissenden, J.E., Caras, I., Thelander, L. and Francke, U. (1988) The structural gene for the M1 subunit of ribonucleotide reductase maps to chromosome 11, band p15, in human and to chromosome 7 in mouse. *Exp. Cell. Res.* 174:302-8.
 - 10. See: http://shows.med.buffalo.edu/home.html
 - 11. Ali, I., Lidereau, R., Theilley, C. and R. Callahan (1987) Reduction to homozygosity of genes on chromosome 11 in human breast neoplasia. *Science* 238:185-8.
 - 12. Winqvist, R., Mannermaa, A., Alavaikko, et al. (1993) Refinement of regional loss of heterozygosity for chromosome 11p15.5 in human breast tumors. *Cancer Research* 53: 4486-4488.
- 13. Carter, S.L., Negrini, M., Baffa, R., et al. (1994) Loss of heterozygosity at 11q22q23 in breast cancer. *Cancer Research* 54:6270-4.
 - 14. Mitra, A.B., Murty, V.V.V.S., Li, R.G., et al. (1994) Allelotype analysis of cervical carcinoma. *Cancer Research* 54:4481.
 - 15. Fujimori, M., Tokino, T., Hino, O., et al. (1991) Allelotype study of primary heptocellular carcinoma. *Cancer Research* 51: 89-93.
 - 16. Wang, H.P. & C.E. Rogler (1988) Deletions in human chromosomes 11p and 13q in primary hepatocellular carcinomas. *Cytogenetics and Cell Genetics* 48:72-78.
 - 17. Bepler, G. and Garcia-Blanco, M.A. (1994) Three Tumor Suppressor Regions on Chromosome 11p Identified by High Resolution Deletion Mapping in Human Non-

10

15

25

- Small Cell Lung Cancer. Proc. Natl. Acad. Sci. U.S.A. 91:5513-7.
- 18. Iizuka, M., Sugiyama, Y., Shiraishi, M., et al. (1995) Allelic losses in human chromosome 11 in lung cancers. *Genes, Chromosomes & Cancer* 13:40-46.
- 19. Weston, A., Willey, J.C., Modali, R., et al. (1989) Differential DNA sequence deletions from chromosomes 3, 11, 13 and 17 in squamous cell carcinoma, large-cell carcinoma and adenocarcinoma of the human lung. *Proc. Natl. Acad. Sci. U.S.A.* 86:5099-5103.
- 20. Kiechle-Schwartz, M., Bauknecht, T., Wienker, T., et al. (1993) Loss of Constitutional Heterozygosity on Chromosome 11p in Human Ovarian Cancer. *Cancer* 72:2423-32.
- 21. Viel, A., Giannini, F., Tumiotti, L., Sopracordevole, F., Visentin, M.C. and M. Boiocchi (1992) Chromosomal localization of two putative 11p oncosuppressor genes involved in human ovarian tumors *British Journal of Cancer* 66: 1030-1036.
- 22. Baffa, R., Negrini, M., Mandes, B., et al. (1996) Loss of heterozygosity for chromosome 11 in adenocarcinoma of the stomach. *Cancer Research* 56: 268-72.
- 23. Lothe, R.A., Hastie, N., Heimdal, K., et al. (1993) Frequent loss of 1p13 and 11p15 loci in male germ cell tumors. *Genes, Chromosomes & Cancer* 7:96-101.
- 24 Smith, R.C., and Rukstalis, D.B. (1995) Frequent Loss of Heterozygosity at 11p Loci in Testicular Cancer. *The Journal of Urology* 153:1684-7.
- 25. Shaw, M.E. and Knowles, M.A. (1995) Deletion Mapping of Chromosome 11 in Carcinoma of the Bladder. *Genes, Chromosomes & Cancer* 13:1-8.
 - 26. Shibagaki, I., Shimada, Y., Wagata, T., et al. (1994) Allelotype analysis of esophageal squamous cell carcinoma. *Cancer Research* 54: 2996-3000.
 - 27. Ahuja, H.G., Foti, A., Zhou, D.J. and M.J. Cline (1990) Analysis of proto-oncogenes in acute myeloid leukemia: loss of heterozygosity for the Ha-ras gene. *Blood* 75: 819-822.
 - 28. Yamaguchi, T., Toguchida, J., Yamamuro, T., et al. (1992) Allelotype analysis in osteosarcoma: frequent allele loss on 3q, 13q, 17p and 18q. *Cancer Res.* 52: 2419.

10

15

20

25

Example 13: Thymidylate Synthase (TS) - Target Gene VARIA250

Thymidylate Synthase is essential for cell growth

Human thymidylate synthase (TS) catalyzes the formation of thymidine monophosphate (dTMP) from deoxyuridine monophosphate (dUMP) by transfer of a methyl group from N5,N10-methylenetetrahydrofolate to carbon 5 of dUMP. This is the sole *de novo* pathway to dTMP, an essential precursor for DNA synthesis. TS also plays an important role in balancing the four nucleotide precursors for DNA polymer synthesis (1). Thus TS is an attractive target for antiproliferative drugs. (*See* Biochemistry by C.K. Mathews and K.E. van Holde, Benjamin/Cummings Publishing Company, Redwood City, 1990, pages 763-768, for a fuller account of thymidylate synthase function.)

Like some other growth associated genes involved in DNA synthesis, thymidylate synthase is expressed in proliferating cells at 20-40 fold higher levels than in quiescent cells. Increased expression occurs at the G1-S transition of the cell cycle when quiescent cells are stimulated with serum. Levels of thymidylate synthase are finely controlled by autoregulatory feedback loops wherein TS protein regulates the transcription, stability and translational efficiency of TS mRNA (2). Transcription increases by only 2-4 fold, so posttranscriptional events constitute the predominant regulatory mechanisms (3). One mechanism of 5-FU resistance is increased expression of TS Mrna.

Thymidylate synthase is the target of 5-fluorouracil (5-FU), a potent antineoplastic compound. Once inside cells 5-FU is ribosylated and phosphorylated to 5-fluoro-2'-deoxyuridine 5'-monophosphate (F-dUMP), which acts as an inhibitory transition state analog of TS when bound in the presence of the enzyme's second substrate, N5,N10-methylenetetrahydrofolate. (5-FU is also incorporated into both DNA and RNA,

PCT/US98/05419

232/116

augmenting its toxicity.) 5-FU induces partial responses in 10-30% of patients with a variety of cancers, including metastatic breast and gastrointestinal tract cancers (4). While 5-FU is a potent antiproliferative agent in tissue culture cells, as with most antineoplastic drugs, its clinical utility is limited by lack of discrimination between normal cells and tumor cells: common toxic effects include stomatitis, diarrhea, bone marrow suppression, hair loss and occasionally cardiac and neurologic symptoms.

The human thymidylate synthase gene has sequence variances

WO 98/41648

5

10

15

20

25

The sequence of a human thymidylate synthase cDNA was determined by Takeishi et al. (5), who later determined the genomic sequence as well (6). We undertook a systematic search for DNA sequence variance by analysing 36 unrelated individuals using the single strand conformation polymorphism. Primers were designed using the sequence of Takeishi et al. (5). SSCP analysis revealed 3 DNA fragments having sequence variances, and subsequent DNA sequence analysis showed that nucleotides 1066 (C vs. T), 1136 (A vs. G) and 1497 (A vs. T) vary among normal individuals as shown in the Target Summary Table. All three sequence variances are in the 3' untranslated region of the gene. The nucleotide 1066 and 1497 sequence variances are in complete linkage disequilibrium in the 36 individuals examined. Both alleles of all three sequence variances were detected in North American Whites, North American Blacks, Chinese, Japanese, Arabs and Indians.

Another TS sequence variance has been described by Berger and colleagues (7-9). They detected a T to C change at nucleotide 276 of the TS gene, resulting in the substitution of histidine for an evolutionarily conserved tyrosine at residue 33 of TS protein. So far the histidine allele has been detected in only one cell line, HCT116 (7). The rare his-33 form of the protein is 3-4 fold more resistant to FdUrd than the tyr-33 form, due to an 8 fold lower catalytic efficiency (kcat), suggesting that histidine at residue 33 perturbs the structure of the TS active site (9)

The human thymidylate synthase gene maps to chromosome 18p11.32

The gene for human thymidylate synthase was initially mapped to the long arm of chromosome 18 (18q21.31-qter) by somatic cell hybrid analysis (10), however two subsequent reports place the gene in band 18p11.32 using fluorescence *in situ* hybridization (11,12).

Chromosome band 18p11.32 is a site of loss of heterozygosity

The long arm of chromosome 18 contains the DCC (deleted in colon cancer) candidate tumor suppressor gene and has been well studied in a variety of tumors. The short arm (18p), where TS apparently resides, has not been studied as extensively. The available data suggests there is LOH in approximately 45% of colon cancers (13) and 25-30% of cervical (14), head and neck (15), lung (16) and ovarian (17) cancers and sarcomas.

LOH has also been described in breast, brain, esophagus, kidney and prostate cancers (0-15%). 18p has not been studied for allele loss in several other major cancers, including bladder, leukemia, lymphoma, liver, pancreas, stomach and testicular cancers.

20 References

- 1. Chu, E., Koeller, D.M., Casey, J.L., et al. (1991) Autoregulation of human thymidylate synthase messenger RNA translation by thymidylate synthase. *Proc. Natl. Acad. Sci. U.S.A.* 88: 8977-81.
- Seno, T., Ayusawa, D., Shimizu, K., et al. (1985) in de Serres, F.J. (ed.) Genetic
 Consequences of Nucleotide Pool Imbalance, Plenum Publishing Company, New York, pp. 241-263.
 - 3. Johnson, L.F. (1994) Posttranscriptional regulation of thymidylate synthase gene expression. *Journal of Cellular Biochemistry* 54: 387-392.

15

25

- 4. Calabresi, P. and B. Chabner (1996) in Hardman, J.G., Limbird, L.E., et al. (eds.) Goodman and Gilman's The Pharmacological Basis of Therapeutics, McGraw Hill, New York, pp. 1247-1251.
- 5. Takeishi, K., Kaneda, S., Aysawa, D., Shimizu, K., Gotoh, O. and T. Seno (1985) Nucleotide sequence of a functional cDNA for human thymidylate synthase. *Nucleic Acids Research* 13: 2035-2043.
- 6. Kaneda, S., Nalbantoglu, K., Takeishi, K., et al. (1990) Structural and functional analysis of the human thymidylate synthase gene. *Journal of Biological Chemistry* 265: 20277-84.
- Barbour, K.W., Berger, S.H. and S.G. Berger (1990) Single amino acid substitution defines a naturally occurring genetic variant of human thymidylate synthase. *Molecular Pharmacology* 37: 515-518.
 - 8. Barbour, K.W., Hoganson, D.K., Berger, S.H. and F.G. Berger (1992) A naturally occurring tyrosine to histidine replacement at residue 33 of human thymidylate synthase confers resistance to 5-fluoro-2'-deoxoyuridine in mammalian and bacterial cells. *Molecular Pharmacology* 42: 242-248
 - 9. Hughey, C.T., Barbour, K.W., Berger, F.G. and S.H. Berger (1993) Functional effects of a naturally occurring amino acid substitution in human thymidylate synthase. *Molecular Pharmacology* 44: 316-323.
- 20 10. Nussbaum, R.L., McCarrick-Walmsley, R., Lesko, J.G., et al. (1985) Thymidylate synthase deficient Chinese hamster cells: a selection system for human chromosome 18 and experimental system for the study of thymidylate synthase regulation and fragile X expression. American Journal of Human Genetics 37: 1192-1205.
 - 11. Hori, T., Takahashi, E., Ayusawa, D., et al. (1990) Regional assignment of the human thymidylate synthase gene to chromosome band 18p11.32 by nonisotopic *in situ* hybridization. *Human Genetics* 85: 576-580.
 - 12. Silverman, G.A., Kuo, W.-L., Taillon-Miller, P. and J.W. Gray (1993) Chromosomal reassignment: YACs containing both YES1 and thymidylate synthase map to the short arm of chromosome 18. *Genomics* 15: 442-445.

- 13. Vogelstein, B., Fearon, E.R., Kern, S.E., et al. (1989) Allelotype of colorectal carcinomas. *Science* 244: 207-211.
- 14. Mullokandov, M.R., Kholodilov, N.G., Atkin, N.B., et al. (1996) Genomic Alterations in cervical carcinoma: losses of chromosome heterozygosity and human papilloma virus tumor status. *Cancer Research* 56: 197-205.
- 15. Nawroz, H., van der Riet, P., Hruban, R.H., et al. (1994) Allelotype of head and neck squamous cell carcinoma. *Cancer Research* 54: 1152-55.
- 16. Allelotype of non-small cell lung carcinoma comparison between loss of heterozy-gosity in squamous cell carcinoma and adenocarcinoma. *Cancer Research*: 52: 2478-81.
- 17. Abeln, E.C.A., Kuipers-Dijkshoom, N.J., Berns, E.M.J.J., et al. (1995) Molecular genetic evidence for unifocal origin of advanced epithelial ovarian cancer and for minor clonal divergence. *British Journal of Cancer* 72: 1330-1336.

10

5

Example 14: Cytidine Triphosphate Synthetase (CTPS) - Target Gene VARIA260

Cytidine Triphosphate Synthetase is essential for cell growth

Human cytidine triphosphate synthetase catalyzes the glutamination of UTP to form CTP. The reaction is: UTP + ATP + glutamine --> CTP + ADP + Pi + glutamate. This is the rate limiting step in the synthesis of cytidine nucleotides from both the *de novo* and uridine salvage synthesis routes (see ref. 1 and references therein). CTPS also plays a vital regulatory function in balancing nucleotide pools for DNA polymer synthesis; it is allosterically regulated by CTP (negatively) and GTP (positively).

There is compelling evidence that CTPS is essential for cell survival:

CTPS is evolutionarily conserved in yeast and bacteria, with a high degree of amino acid identity in regions mediating allosteric regulation and catalysis (1-

10

15

20

25

3). (Another example: the human and hamster enzymes are identical in length and 98% amino acid identical over 591 amino acids.)

Mutant hamster cells lacking functional CTPS need exogenous cytidine to survive (3).

There is no known human deficiency disease of CTPS.

CTPS function is increased in proliferating cells (4).

Thus CTPS is an attractive target for antiproliferative drugs. Cyclopentyl cytosine (CPE-C) is a synthetic cytidine analog in which a cyclopentyl group replaces the furan ring of the ribose sugar. CPE-C has antineoplastic and antiviral effects in animal models (5). The drug is kinased intracellularly to the triphosphorylated nucleotide form (CPE-CTP). Exposure of cells to CPE-C leads to rapid depletion of CTP pools, as a result of inhibition of CTPS by CPE-CTP (6,7). Upregulation of CTP synthetase, or loss of negative allosteric modulation by CTP is associated with resistance to the cancer chemotherapy drugs arabinosyl cytosine (ara-C), 5-fluorouracil and other cytotoxic nucleoside analogs as well as alkylating agents (3).

The human cytidine triphosphate synthetase gene has sequence variances

The sequence of a human cytidine triphosphate synthetase cDNA was determined by Yamauchi et al. (1), who later determined the genomic sequence as well (2). We undertook a systematic search for DNA sequence variance by analysing 36 unrelated individuals using the single strand conformation polymorphism technique. Primers were designed using the sequence of Yamauchi et al. (1). SSCP analysis revealed 3 DNA fragments having sequence variances, and subsequent DNA sequence analysis showed that nucleotides 576 (A vs. G), 2093 (C vs. T) and 2135 (G vs. A) vary among normal individuals as shown in the Target Summary Table. The nucleotide 576 sequence variance is a silent substitution in the coding region, while the latter two sequence variances are in the 3' untranslated region of the cDNA. All three sequence

variances were detected at low frequency in the panel of 36 individuals (3-8%), however all but one of the heterozygotes is Asian, and it seems likely that a larger survey of Asian populations would show higher allele frequencies in Chinese and other groups. For example among the four Chinese in the panel two (50%) are heterozygous for the residue 2135 sequence variance, and one (25%) is heterozygous for the nt 576 sequence variance. Also, the one Cambodian in the panel is heterozygous for both the 2093 and 2135 sequence variances.

The human cytidine triphosphate synthetase gene maps to chromosome 1p34.1

10

5

The gene for human cytidine triphosphate synthetase has been mapped to 1p34.1 by somatic cell hybrid analysis (2).

Chromosome band 1p34.1 is a site of frequent loss of heterozygosity

15

20

The short arm of chromosome 1 is comparatively well investigated for allele loss, especially in breast and colon cancers. The 1p35-32 and 1p22-13 regions flank 1p34.1 and are the best available markers for LOH on 1p. Studies of these regions show 30-50% LOH frequency in breast cancer (8-12), 41-75% in glioma (a brain cancer subtype) (13), 20-40% in colon cancer (14,15), ~50% in stomach cancer (16), ~20% in lung cancer (17) and 20-30% in ovarian cancer (18). High frequency LOH has been detected in several uncommon cancers such as pheochromocytoma (50-86%) and neuroblastoma (~50%). Most other common cancers have not been adequately investigated to assess LOH frequency in this region.

25

References

1. Yamauchi, M., Yamauchi, N. and M. Meuth (1990) Molecular cloning of the human CTP synthetase gene by functional complementation with purified human metaphase

15

25

chromosomes. EMBO Journal 9: 2095-2099.

- 2. Yamauchi, M., Yamauchi, N., Phear, G., et al. (1991) Genomic organization and chromo-somal localization of the human CTP synthetase gene(CTPS). *Genomics* 11: 1088-96.
- 3. Whelan, J., Phear, G., Yamauchi, M. and M. Meuth (1993) Clustered base substitutions in CTP synthetase conferring drug resistance in Chinese hamster ovary cells. *Nature Genetics* 3: 317-322.
 - 4. van den Berg, A., van Lenthe, H., Busch, S., et al. (1993) Evidence for transformation related increase in CTP synthetase activity *in situ* in human lymphoblastic leukemia. *European Journal of Biochemistry* 216: 161-167.
 - 5. Marquez, V.E., Lim, M.-I., Treanor, S.P., et al. (1988) Cyclopentylcytosine: a carbocyclic nucleoside with antitumor and antiviral properties. *Journal of Medical Chemistry* 31: 1687-94.
 - 6. Kang, G.J., Cooney, D.A., Moyer, J.D., et al. (1989) Cyclopentenyl triphosphate: formation and inhibition of CTP synthetase. *Journal of Biological Chemistry* 264: 713-718.
 - 7. Glazer, R.I., Knode, M.C. Lim, M.-I., and V.E. Marquez (1985) Cyclopentyl cytidine analogue: an inhibitor of cytidine triphosphate synthesis in human colon carcinoma cells. *Biochemical Pharmacology* 34: 2535-2539.
- 8. Bieche I, Champeme MH, Matifas F, Cropp CS, Callahan R, Lidereau R. (1993)
 Two distinct regions involved in 1p deletion in human primary breast cancer. *Cancer Res.* 53:1990-4.
 - 9. Borg A, Zhang QX, Olsson H, Wenngren E. (1992) Chromosome 1 alterations in breast cancer: allelic loss on 1p and 1q is related to lymphogenic metastases and poor prognosis. *Genes Chromosomes & Cancer*. 5:311-20.
 - 10. Sato T, Tanigami A, Yamakawa K, et al. (1990) Allelotype of breast cancer: cumulative allele losses promote tumor progression in primary breast cancer. *Cancer Res.* 50:7184-9.
 - 11. Devilee P, van Vliet M, Bardoel A, et al. (1991) Frequent somatic imbalance of

10

20

marker alleles for chromosome 1 in human primary breast carcinoma. *Cancer Res.* 51:1020-5.

- 12. Loupart ML, Armour J, Walker R, Adams S, Brammar W, Varley J. (1995) Allelic imbalance on chromosome 1 in human breast cancer. I. Minisatellite and RFLP analysis. *Genes Chromosomes & Cancer*. 12:16-23.
- 13. Reifenberger, J., Reifenberger, G., Liu, L., et al. (1994) Molecular genetic analysis of oligodendroglial tumors shows preferential allelic deletions on 19q and 1p. American Journal of Pathology 145: 1175-1190.
- 14 Meling GI, Lothe RA, Borresen AL, et al. (1991) Genetic alterations within the retinoblastoma locus in colorectal carcinomas. Relation to DNA ploidy pattern studied by flow cytometric analysis. *Br J Cancer*. 64:475-80.
 - 15. Lothe RA, Nakamura Y, Woodward S, Gedde DT, Jr., White R. (1988) VNTR (variable number of tandem repeats) markers show loss of chromosome 17p sequences in human colorectal carcinomas. *Cytogenet Cell Genet*. 48:167-9.
- 16. Ezaki, T., Yanagisawa, A., Ohta, K., et al. ((1996) Deletion mapping on chromosome 1p in well-differentiated gastric cancer. *British Journal of Cancer* 73: 424-428.
 - 17. Hiyama K, Ishioka S, Shirotani Y, et al. (1995) Alterations in telomeric repeat length in lung cancer are associated with loss of heterozygosity in p53 and Rb. *Oncogene*. 10:937-44.
 - 18. Yang-Feng TL, Han H, Chen KC, et al. (1993) Allelic loss in ovarian cancer. *Int J Cancer*. 54:546-51.

25 Example 15: Cysteinyl tRNA Synthetase (CARS) - Target Gene VARIA301

The human cysteinyl tRNA synthetase gene is essential for cell survival

Cysteinyl-tRNA synthetase (CARS) catalyzes ATP dependent covalent attachment of

WO 98/41648 PCT/US98/05419

216 232/116

cysteine to its cognate tRNA to form cysteinyl-tRNA. In the absence of cysteinyl-tRNA, protein synthesis is blocked. Since Cysteinyl-tRNA synthetase is a single copy gene in man, inhibition of its function is expected to be cell lethal. This has been shown for other tRNA synthetases (summarized above).

5

The human cysteinyl-tRNA synthetase gene and mRNA have sequences variances

A human cDNA encoding cysteinyl tRNA synthetase (CARS) was cloned based on the similarity of a human expressed sequence tag (EST) to E. coli cysteinyl tRNA

10

synthetase (1). The published human CARS cDNA is 2048 nucleotides in length and includes a 30 nucleotide 5' untranslated region followed by an open reading frame of 1914 nucleotides and a 3' untranslated region of 134 nucleotides (1). An EMBL/GENBANK submission (accession # L06845) by the authors of ref. 1 includes a 3' untranslated region 423 nucleotides longer than the published sequence, but lacks 19 consecutive A nucleotides after position 2029 (making a net increase of: 423 - 19 = 404 nucleotides, and a composite cDNA of: 2048 + 404 = 2452 nucleotides in length.

15

We have confirmed the existence of 2452 nt transcripts by PCR amplification of reverse transcribed mRNA.) We designed primers as shown on the annotated cDNA

sequence and screened the composite 2452 nt cDNA for sequence variance in 36

20

unrelated individuals by the single strand conformation polymorphism (SSCP) technique. Two sequence variances were identified. One of the sequence variances,

located in the 5' untranslated region, was below the desired level of 20% heterozygosity. The other sequence variance is a C vs. T transition near the 3' end of

25

The human cysteinyl tRNA synthetase protein has sequence variances

the coding sequence at nucleotide 1739 (see annotated sequence).

The deduced amino acid sequence of the human CARS gene encodes a protein of 638 amino acids which probably functions as a monomer, by analogy to related synthetases. The deduced protein contains two sequence motifs, HIGH (residues 64-

67) and KMSKS (residues 406-410), which define Class I synthetases (see ref. 2 for background information on tRNA synthetases). These two conserved motifs form an ATP binding fold (the Rossman fold) in the amino terminal half of the protein. Cytosine at nucleotide 1739 encodes proline at residue 622 of the protein, while thymine at nucleotide 1739 encodes leucine. The pro/leu amino acid sequence variance is a mere 16 residues from the C terminus of the protein. The C-terminal portion of CARS, by analogy to other class I synthetases, contains the tRNA binding site.

Frequency of CARS heterozygotes

The frequency of heterozygotes for the nucleotide 1739 sequence variance is ~45-50% in all major racial groups surveyed (see accompanying table), including North American Whites (8/15=53%), North American Blacks (2/4=50%), Chinese (2/4=50%), Swedish (127/344=37%) and Japanese (1/4=25%). The wide population distribution of both alleles suggests that other population groups will also have a high frequency of heterozygotes.

Gene Mapping of CARS to 11p15.5

20

25

5

10

15

Human CARS cDNA has been mapped to chromosome 11p15.5 by screening human X Chinese hamster somatic cell hybrids informative for all human chromosomes, and by fluorescence *in situ* hybridization (3). Both mapping techniques were conclusive in showing only one locus for human CARS. Detailed physical maps of 11p15.5 have subsequently allowed precise localization of the CARS gene relative to other DNA markers (4).

LOH at 11p15.5 is well documented in many cancer types

The short arm of chromosome 11, and particularly the 11p15.5 region, is deleted in a

variety of human cancers, including (but not limited to) ovarian (18 - 50% LOH), non-small cell lung (22 - 71%), breast (12 - 33%), bladder (40 -50%), esophageal (18 - 40%) and testicular cancers (18 - 66%) (refs. 5-12). Many deletions in the 11p15.5 region span relatively short chromosomal segments (2 - 10 megabases; see ref. 8). Using the specific variances identified in the CARS gene as markers for heterozygosity, we have determined that LOH occurs in 10/20 ovarian cancers (50%) and 10/52 non-small cell lung cancers (19%).

Assays for human CARS inhibitors

10

15

20

5

There is no published work on the protein encoded by the putative human CARS cDNA, nor on any other eukaryotic CARS protein, however the extensive characterization of other Class I synthetases from both prokaryotes and eukaryotes provides a template for modeling the structure of human CARS. (For an example of how this can be done see ref..14, in which the three dimensional structure of human alanyl-tRNA synthetase has been modeled up to amino 249 by neural net software and multiple alignments of partial and complete human AARS sequences with heterologous prokaryotic class II synthetases for which crystal structures exist.) With respect to the C-terminal location of the variant amino acid residue in human CARS, it is worth noting that single amino acid substitutions in the C-terminal region of alanyl tRNA synthetase can have greater than 100 fold effects on catalytic activity (15).

References

25

- 1. Wasmuth, J.J. Cruzen, M. E. and S.M. Arfin (1994) Nucleotide and deduced amino acid sequence of human cysteinyl-tRNA synthetase. *DNA Sequence* 4:243-248.
- 2. Moras, D. (1992) Structural and functional relationships between aminoacyl-tRNA synthetases. *Trends in Biochemical Sciences* 17: 159-164.
- 3. Cruzen, M.E., Bengtsson, U., McMahon, J., Wasmuth, J.J. and S.M. Arfin (1993)

15

Assignment of the cysteinyl-tRNA synthetase gene (CARS) to 11p15.5. *Genomics* 15: 692-693.

- 5. Winqvist, R., Mannermaa, A., Alavaikko, M., Blanco, G., Taskinen, P.J., Kiviniemi, H., Newsham, I. and W. Cavenee (1993) Refinement of regional loss of heterozygosity for chromosome 11p15.5 in human breast tumors. *Cancer Research* 53: 4486-4488.
- 6. Kiechle-Schwartz, M., Bauknecht, T., Wienker, T., et al. (1993) Loss of Constitutional Heterozygosity on Chromosome 11p in Human Ovarian Cancer. *Cancer* 72:2423-32.
- 7. Viel, A., Giannini, F., Tumiotti, L., Sopracordevole, F., Visentin, M.C. and M. Boiocchi (1992) Chromosomal localisation of two putative 11p oncosuppressor genes involved in human ovarian tumors *British Journal of Cancer* 66: 1030-1036.
 - 8. Bepler, G. and Garcia-Blanco, M.A. (1994) Three Tumor Suppressor Regions on Chromosome 11p Identified by High Resolution Deletion Mapping in Human Non-Small Cell Lung Cancer. *Proc. Natl. Acad. Sci. U.S.A.* 91:5513-7.
 - 9. Iizuka, M., Sugiyama, Y., Shiraishi, M., Jones, C. and T. Sekiya (1995) Allelic losses in human chromosome 11 in lung cancers. *Genes, Chromosomes & Cancer* 13:40-46. 10. Shaw, M.E. and Knowles, M.A. (1995) Deletion Mapping of Chromosome 11 in Carcinoma of the Bladder. *Genes, Chromosomes & Cancer* 13:1-8.
- 20 11. Smith, R.C., and Rukstalis, D.B. Frequent Loss of Heterozygosity at 11p Loci in Testicular Cancer. *The Journal of Urology* 153:1684-7, 1995.
 - 12. Shibagaki, I., Shimada, Y., Wagata, T., Ikenaga, M., Imamura, M. and K. Ishizaki (1994) Allelotype analysis of esophageal squamous cell carcinoma. *Cancer Research* 54: 2996-3000.
- 13. Shiba, K., Suzuki, N., Shigesada, K., Namba, Y., Schimmel, P. and T. Noda (1994) Human cytoplasmic isoleudyl-tRNA synthetase: selective divergence of the anticodon-binding domain and acquisition of a new structural unit. *Proc. Natl. Acad. Sci. U.S.A.* 91:7435-7439.
 - 14. Shiba, K., Ripmaster, T., Suzuki, N., Nichols, R., Plotz, P., Noda, T. and P.

10

15

20

25

Schimmel (1995) Human alanyl-tRNA synthetase: conservation in evolution of catalytic core and microhelix recognition. Biochemistry 34: 10340-10349.

15. Wu, M.-X., Filley, S.J., Xiong, J., Lee, J.J. and K.A.W. Hill (1994) A cysteine in the C-terminal region of alanyl-tRNA synthetase is important for aminoacylation activity. *Biochemistry* 33: 12260-12266.

Example 16: Glutamyl-Prolyl tRNA Synthetase (EPRS): - Target Gene VARIA300

The human glutamyl-prolyl tRNA synthetase gene is essential for cell survival

Glutamyl-prolyl-tRNA synthetase (EPRS) catalyzes ATP dependent covalent attachment of glutamine and proline to their cognate tRNAs to form glutamyl-tRNA and prolyl-tRNA. In the absence of glutamyl-tRNA or prolyl-tRNA, protein synthesis is blocked. Since glutamyl-prolyl-tRNA synthetase is a single copy gene in man, inhibition of its function is expected to be cell lethal. This has been shown for other tRNA synthetases (summarized above).

The human glutamyl-prolyl tRNA synthetase gene, mRNA and protein have sequence variances

A human cDNA encoding glutamyl-prolyl tRNA synthetase (EPRS) was initially misidentified as glutaminyl-tRNA synthetase (1) based on misleading sequence alignments with bacterial and yeast glutaminyl-tRNA synthetase (2). Subsequently, biochemical studies of the protein encoded by a *D. melanogaster* gene ~70% identical to the human gene demonstrated glutamyl (not glutaminyl) tRNA synthetase activity, and also showed that a single gene encodes both glutamyl- and prolyl-tRNA synthetases in the fly (3). These observations eventually led to the realization that

human EPRS is also a single polypeptide containing two synthetases (2). The aminoacyl tRNA synthetases are divided into two classes (see *Background on tRNA Synthetases*, above). Glutamyl-tRNA synthetase belongs to Class I while Prolyl-tRNA synthetase belongs to class II. Thus the two halves of EPRS evolved independently and likely represent an evolutionarily recent fusion. The published human EPRS cDNA is 4,586 nt long and includes a 5' untranslated region of 58 nt followed by an open reading frame of 4320 nt and a 3' untranslated sequence of 208 nt (1). The gene encodes a polypeptide of 1440 amino acids. The glutamyl-tRNA synthetase activity is encoded by an imprecisely defined segment at 5' end of the gene probably spanning at least amino acids 105-426, while the prolyl-tRNA synthetase activity is encoded by a segment likely including residues 942-1369 at the 3' end of the gene (2). The two synthetase moieties are connected by a central domain of unknown function. It has been speculated that the central domain may attach the enzyme to the cytoskeleton or to other aminoacyl-tRNA synthetases in a multienzyme complex (2, 3).

15

20

25

10

5

The human glutamyl-prolyl-tRNA synthetase gene and mRNA have sequence variances. We designed primers and screened the 4586 nt cDNA for sequence variance in 36 unrelated individuals by the single strand conformation polymorphism technique. Seven sequence variances were identified, four located in the coding sequence and three located in the 3' untranslated region. As shown on the Annotated Glutamyl-Prolyl tRNA Synthetase cDNA Sequence and in the Target Summary Page, the sequence variance nucleotides are 2520 (C vs. A), 2944 (G vs. A), 2963 (C vs. T), 2969 (A vs. G), 3247 (A vs. G), 4459 (G vs. A) and 4506 (G vs. A). The sequences flanking the alternate allelic forms and their frequencies of occurrence are shown on the Target Summary Page. Less than 10% of individuals surveyed are heterozygous for sequence variances at 2520, 2944 and 2963. Heterozygotes for the other 4 sequence variances occur more frequently and appear to be widely distributed in the surveyed populations (see below).

232/116

The human glutamyl-prolyl tRNA synthetase protein has sequence variances. Three nucleotide sequence variances, at 2520, 2963 and 2969, alter the amino acid coding sequence of EPRS at residues 821 (pro/his), 969 (his/tyr) and 971 (ile/val). The residue 821 his and 969 tyr alleles are relatively rare, with fewer than 10% heterozygotes in the surveyed populations. The more common residue 971 sequence variance lies in the PRS domain of the protein, near one of the widely conserved defining motifs for class II tRNA synthetases.

EPRS heterozygotes are frequent in non-Asian populations. While the overall frequency of residue 971 heterozygotes is 8/36 (24%), the frequency of heterozygotes varies among different populations. For example, there are no heterozygotes among 10 Asians surveyed (Chinese, Japanese, Filipino and Korean), while 8/26 (31%) of non-Asians, including North American Whites, Blacks and Hispanics, are heterozygotes.

15

10

5

The EPRS Gene Maps to 1q41-q42

Human EPRS cDNA has been mapped to chromosome 1q41-42 by screening human X Chinese hamster somatic cell hybrids informative for all human chromosomes, and by fluorescence *in situ* hybridization (3). Both mapping techniques were conclusive in showing only one locus for human EPRS.

25

20

Loss of heterozygosity at 1q41-42 is documented in several cancer types. 17-25% of breast cancers have allele loss in the 1q41-q42 region (4, 5), 29-46% of colon cancers (6, 7) and 17-26% of cervical cancers (8). One report describes 27% LOH in stomach cancer (9). One or two studies of brain, esophageal, kidney, liver and ovarian cancers also report LOH. No studies of LOH in the 1q41-q42 region have been reported in bladder, endocrine, head and neck, lung, or pancreas cancers or in leukemia or lymphoma.

232/116

Antisense considerations The sequence variances at 2963 and 2969 are close enough that a 20-mer antisense oligonucleotide could easily span them. Such an oligonucleotide should afford greater allele discrimination than is possible with a single nucleotide difference. However, the 2963 sequence variance is fairly rare (<10% heterozygotes) and not in linkage disequilibrium with the 2963 sequence variance, so there are more than two haplotypes in the populations tested.

References

5

- 1. Fett, R. and R. Knippers (1991) The primary structure of human glutaminyl tRNA synthetase. *Journal of Biological Chemistry* 266: 1448-1455.
 - 2. Cerini, C., Kerjan, P., Astier, M., Gratecos, D., Mirande, M. and M. Semeriva (1991) A component of the multisynthetase complex is a multifunctional aminoacyltRNA synthetase. *The EMBO Journal* 10: 4267-4277.
- 3. Kaiser, E., Hu, B., Becher, S., Eberhard, D., et al. (1994) The human EPRS locus (formerly the QARS locus): a gene encoding a class I and a class II aminoacyl-tRNA synthetase. *Genomics* 19: 280-290.
 - 4. Journal of The National Cancer Institute 84: 506.
 - 5. Cancer Research 51: 1020.
- 20 6. International Journal of Cancer 53: 382.
 - 7. Genes, Chromosomes & Cancer 12: 16.
 - 8. Cancer Research 56: 197.
 - 9. Cancer Research 52: 3099.
- Shiba, K., Ripmaster, T., Suzuki, N., Nichols, R., Plotz, P., Noda, T. and P.
 Schimmel (1995) Human alanyl-tRNA synthetase: conservation in evolution of catalytic core and microhelix recognition. Biochemistry 34: 10340-10349.

Example 17: Alanyl-tRNA Synthetase (AARS) - Target Gene VARIA304

The human glutamyl-prolyl tRNA synthetase gene is essential for cell survival

Alanyl-tRNA synthetase (AARS) catalyzes ATP dependent covalent attachment of alanine to its cognate tRNA to form alanyl-tRNA. In the absence of alanyl-tRNA, protein synthesis is blocked. Since alanyl-tRNA synthetase is a single copy gene in man (see below) inhibition of its function is expected to be cell lethal. This has been shown for other tRNA synthetases (summarized above).

The human alanyl-tRNA synthetase gene and mRNA have sequence variances

10

5

A human cDNA encoding alanyl tRNA synthetase (AARS) was cloned by Shiba et al. (1) using cross species PCR: AARS sequences from four evolutionarily distant species were compared and primers were designed to conserved regions specific to AARS. The cloned human cDNA is 3344 nt in length and includes a 110 nt 5' untranslated region, an open reading frame of 2904 nt encoding a 968 residue polypeptide, and a 3' untranslated region of 330 nt (ref. 1; Genbank accession D32050).

15

We designed primers. The 3344 nt cDNA was screened for sequence variance in 36 unrelated individuals by the single strand conformation polymorphism (SSCP) technique. One sequence variance was identified, a C νs . T transition at nucleotide 1013, within the coding sequence. The published nucleotide at position 1013 is T (1).

20

25

The frequency of AARS heterozygotes is 25-50% in all populations surveyed. The frequency of heterozygotes for the nucleotide 1013 sequence variance is 57% in the 36 individuals tested. Both alleles are present in all major racial groups surveyed (see Target Gene Summary Table), including North American Whites (9/15=60% heterozygotes), North American Blacks (3/4=75%), Chinese (2/4=50%), Japanese (1/4=25%) and Hispanic (1/2). The wide population distribution of both alleles suggests that other population groups will also have a high frequency of heterozygotes.

10

15

20

25

The AARS gene maps to 16q22

The human AARS cDNA has been mapped to chromosome 16q22 by us and by Nichols et al. (ref. 2). We designed primers to the 3' untranslated region of AARS and used PCR to analyze the National Institute of General Medical Sciences (NIGMS) Human/Rodent Somatic Cell Hybrid Mapping Panel #2 (see page 704 of the NIGMS 1994/1995 Catalog of Cell Lines, available from the Coriell Cell Repository, Camden, NJ). The panel consists of 24 hybrid cell lines, each monochromosomal for one human chromosome. The AARS PCR product mapped to the hybrid containing human chromosome 16. Subsequently we screened the Radiation Hybrid Mapping Panel created at Stanford University (rhserver@shgc.stanford.edu) and distributed by Research Genetics (RH01). The AARS PCR product mapped near D16S496 with a lod score>10. D16S496 is a polymorphic DNA marker at 16q22. The AARS PCR product mapped near D16S496 with a LOD score >10. DH16S496 is a polymorphic DNA marker at 16q22. (See, ref. 29 for a full explanation of modification hybrid mapping.) Similar results were obtained by Nichols et al., who mapped AARS by analysis of the same NIGMS hybrid mapping panel, by PCR mapping in a chromosome 16 regional mapping panel and by fluorescence in situ hybridization to metaphase chromosomes. All mapping techniques were conclusive in showing only one locus for human AARS.

LOH at 16q22 is well documented in many cancer types. Loss of heterozygosity studies of chromosome 16q have principally focused on breast and liver cancers. In six detailed studies of breast cancer in the 16q22 region LOH frequencies of 40-60% have been reported (refs 3-8). 16q22 LOH has ben reported in 25-90% of liver cancers (9-13), with the average around 45%. Less extensive studies of other cancer types report 16q22 LOH in 19% of bladder cancers, 20% of colon cancers (14), 19-27% of esophageal cancers (15), 25% of small cell lung cancers (16), 16-37% of ovarian cancers (17-19) and 22% of uterine cancers (20), and 31-50% of prostate cancers (21-

22).

5

10

15

20

25

References

- 1. Shiba, K., Ripmaster, T., Suzuki, N., Nichols, R., Plotz, P., Noda, T. and P. Schimmel (1995) Human alanyl-tRNA synthetase: conservation in evolution of catalytic core and microhelix recognition. Biochemistry 34: 10340-10349.
- 2. Nichols, R.C., Pai, S.I., Ge, Q., Targoff, I.N., Plotz, P.H. and P. Liu (1995) Localization of two human autoantigen genes by PCR screening and *in situ* hybridization glycyl tRNA synthetase locates to 7p15 and alanyl-tRNA synthetase locates to 16q22. *Genomics* 30:131-132.
- 3. Cleton-Jansen AM, Moerland EW, Kuipers-Dijkshoorn NJ, et al. (1994) At least two different regions are involved in allelic imbalance on chromosome arm 16q in breast cancer. *Genes Chromosom Cancer*. 9:101-7.
- 4. Dorion-Bonnet F, Mautalen S, Hostein I, Longy M. (1995) Allelic imbalance study of 16q in human primary breast carcinomas using microsatellite markers. *Genes Chromosomes Cancer*. 14:171-81.
- 5. Kashiwaba M, Tamura G, Suzuki Y, et al. (1995) Epithelial-cadherin gene is not mutated in ductal carcinomas of the breast. *Jpn J Cancer Res.* 86:1054-9.
- 6. O'Connell P, Pekkel V, Fuqua S, Osborne CK, Allred DC. (1994) Molecular genetic studies of early breast cancer evolution. *Breast Cancer Res Treat*. 32:5-12.
- 7. Sato T, Akiyama F, Sakamoto G, Kasumi F, Nakamura Y. (1991) Accumulation of genetic alterations and progression of primary breast cancer. *Cancer Res.* 51:5794-9.
- 8. Tsuda H, Callen DF, Fukutomi T, Nakamura Y, Hirohashi S. (1994) Allele loss on chromosome 16q24.2-qter occurs frequently in breast cancers irrespectively of differences in phenotype and extent of spread. *Cancer Res.* 54:513-7.
- 9. Fujimori M, Tokino T, Hino O, et al. (1991) Allelotype study of primary hepatocellular carcinoma. *Cancer Res.* 51:89-93.
- 10. Fujimoto Y, Hampton LL, Wirth PJ, Wang NJ, Xie JP, Thorgeirsson SS. (1994) Alterations of tumor suppressor genes and allelic losses in human hepatocellular

20

25

carcinomas in China [see comments]. Cancer Res. 54:281-5.

- 11. Tsuda H, Zhang WD, Shimosato Y, et al. (1990) Allele loss on chromosome 16 associated with progression of human hepatocellular carcinoma. *Proc Natl Acad Sci US A*. 87:6791-4.
- 12. Tsuda H, Oda T, Sakamoto M, Hirohashi S. (1992) Different pattern of chromosomal allele loss in multiple hepatocellular carcinomas as evidence of their multifocal origin. *Cancer Res.* 52:1504-9.
 - 13. Zhang WD, Hirohashi S, Tsuda H, et al. (1990) Frequent loss of heterozygosity on chromosomes 16 and 4 in human hepatocellular carcinoma. *Jpn J Cancer Res.* 81:108-11.
 - 14. Ookawa K, Sakamoto M, Hirohashi S, et al. (1993) Concordant p53 and DCC alterations and allelic losses on chromosomes 13q and 14q associated with liver metastases of colorectal carcinoma. *Int J Cancer*. 53:382-7.
 - 15. Genes, Chromosomes & Cancer 10: 177.
- 16. Yokota J, Wada M, Shimosato Y, Terada M, Sugimura T. (1987) Loss of heterozygosity on chromosomes 3, 13, and 17 in small-cell carcinoma and on chromosome 3 in adenocarcinoma of the lung. *Proc Natl Acad Sci U S A*. 84:9252-6.
 17. Cancer Research 51: 5118.
 - 18. Osborne RJ, Leech V. (1994) Polymerase chain reaction allelotyping of human ovarian cancer. *Br J Cancer*. 69:429-38.
 - 19. Yang-Feng TL, Han H, Chen KC, et al. (1993) Allelic loss in ovarian cancer. *Int J Cancer*. 54:546-51.
 - 20. Okamoto A, Sameshima Y, Yamada Y, et al. (1991) Allelic loss on chromosome 17p and p53 mutations in human endometrial carcinoma of the uterus. *Cancer Res.* 51:5632-5.
 - 21. Carter, B.S., Ewing, C.M., Ward, S.W., et al. (1990) Allelic loss of chromosomes 16q and 10q in human prostate cancer. *Proc Natl Acad Sci U S A*. 87: 8751-8755.
 - 22. Bergerheim, U.S.R., Kunimi, K., Collins, V.P. and P. Ekman (1991) Deletion mapping of chromosomes 8, 10, and 16 in human prostatic carcinoma. *Genes*,

232/116

Chromosomes & Cancer 3: 215-220.

23. Boehnke, M., Lange, K. and D.R. Cox (1991) Statistical methods for multipoint radiation hybrid mapping. *Am. J. Hum. Genet.* 49: 1174-88.

5

Example 18: Threonyl-tRNA Synthetase (TARS) - Target Gene VARIA302

The human threonyl-tRNA synthetase gene is essential for cell survival

10

Threonyl-tRNA synthetase (TARS) catalyzes ATP dependent covalent attachment of threonine to its cognate tRNA to form threonyl-tRNA. In the absence of threonyl-tRNA, protein synthesis is blocked. Threonyl-tRNA synthetase is a single copy gene in man (see below) and inhibition of TARS is cell lethal. This has been shown using the specific TARS inhibitor borrelidin, a threonine analog. Borrelidin resistant CHO cell lines have been isolated; the most resistant lines contain ~60-100 fold more immunologically reactive protein and 10-20 fold higher TARS activity than non-selected CHO cells (1-3).

15

20

The human TARS enzyme is a homodimeric member of the class II tRNA synthetases. The human protein is 53% amino acid identical to *S. cerevisiae* cytoplasmic TARS, 40% amino acid identical to *E. coli* TARS and 39% amino acid identical to yeast mitochondrial TARS. The degree of evolutionary conservation is 52-64% when conservative substitutions are allowed.

25

The human Threonyl-tRNA synthetase gene and mRNA have sequence variances. A human cDNA encoding threonyl tRNA synthetase was cloned by Cruzen and Arfin (GENBANK accession M63180; ref. 2) using anti-TARS antibodies to screen a lgt11 expression library. The cDNA is 2644 nt in length and includes a 138 nt 5' untranslated region, an open reading frame of 2136 nt encoding a 712 residue polypeptide, and a 3'

untranslated region of 370 nt.

We designed primers for amplification. The 2644 nt cDNA was screened for sequence variance in 36 unrelated individuals by the single strand conformation polymorphism (SSCP) technique. Three sequence variances were identified: G vs. A transitions at nucleotides 1608 and 1755 within the coding sequence, and a C vs. T transition at nucleotide 2395 of the 3' untranslated region. None of the sequence variances alters the sense of the coding strand. The published sequence shows G, G and T at the three sequence variance sites

10

5

The frequency of TARS heterozygotes is 25-45% in all populations surveyed. The nucleotide 1608 sequence variance was genotyped only in North American Whites, 45% of whom were heterozygotes. The nucleotide 1608 and 1755 sequence variances were both genotyped in 36 individuals, with overall heterozygosity rates of 31% and 25%, respectively. Both sequence variances were detected in North American Whites, North American Blacks, Hispanics and Chinese. Of 14 North American Whites genotyped at all 3 sequence variance nucleotides, 11 (79%) were heterozygous for a least one polymor-phism (see threonyl tRNA synthetase summary table).

20

15

The TARS gene maps to 5p13-CEN. The human TARS cDNA has been mapped to chromosome 5p13-CEN by analysis of TARS isoelectric focusing patterns in human/Chinese hamster hybrids (). The mapping studies were consistent with one human TARS locus.

25

LOH at 5p13-CEN is documented in several cancer types. The best data on 5p LOH is in cervical cancer where 9 markers have been tested in 3 different studies. The frequency of LOH ranges from 12-57%, averaging ~45%. Other cancers that have been studied are breast (10-24% LOH), head and neck (20% LOH), adenocarcinoma of the lung (40% LOH, but only 5 cancers were studied), melanoma (40%) and ovary (15-

21%).

5

10

15

20

25

Assays for human TARS inhibitors. Human TARS protein is a homodimeric class II synthetase. Antibodies to rat TARS were used to clone the human protein. The high degree of amino acid conservation throughout the protein suggests that it may be possible to create yeast and/or bacterial strains with human CARS.

References

- 1. Gantt, J.S., Bennett, C.A. and S.M. Arfin (1981) Increased levels of threonyl tRNA synthetase in a borrelidin-resistant Chinese hamster ovary cell line. *Proc. Natl. Acad. Sci. U. S. A.* 92: 5367-5370.
 - 2. Gerken, S.C. and S.M. Arfin (1984) Chinese hamster ovary cells resistant to borrelidin overproduce threonyl-tRNA synthetase. *The Journal of Biological Chemistry* 259: 9202-9206.
- 3. Kontis, K.J. and S.M. Arfin (1989) Isolation of a cDNA clone for human threonyl tRNA synthetase: amplification of the structural gene in borrelidin resistant cell lines. *Molecular and Cellular Biology* 9: 1832-1838.
 - 4. Cruzen, M.E. and S.M. Arfin (1991) Nucleotide and deduced amino acid sequence of human threonyl-tRNA synthetase reveals extensive homology to the Escherichia coli and yeast enzymes. *The Journal of Biological Chemistry* 266: 9919-9923.
 - 5. Gerken, S.C., Wasmuth, J.J. and S.M. Arfin (1986) Threonyl-tRNA synthesis gene maps close to leucyl-tRNA synthesis gene on human chromosome 5. *Somatic Cell and Molecular Genetics* 12: 519-522.
 - 6. Mitra AB, Murty VV, Singh V, et al. (1995) Genetic alterations at 5p15: a potential marker for progression of precancerous lesions of the uterine cervix. *J Natl Cancer Inst.* 87:742-5.
 - 7. Mitra AB, Murty VV, Li RG, Pratap M, Luthra UK, Chaganti RS. (1994) Allelotype analysis of cervical carcinoma. *Cancer Res.* 54:4481-7.
 - 8. Mullokandov MR, Kholodilov NG, Atkin NB, Burk RD, Johnson AB, Klinger HP.

10

20

- (1996) Genomic alterations in cervical carcinoma: losses of chromosome heterozygosity and human papilloma virus tumor status. *Cancer Res.* 56:197-205.
- 9. Larsson C, Bystrom C, Skoog L, Rotstein S, Nordenskjold M. (1990) Genomic alterations in human breast carcinomas. *Genes Chromosomes Cancer*. 2:191-7.
- 10. Cancer Research 54:1152
 - 11. Wieland I, Bohm M, Arden KC, et al. (1996) Allelic deletion mapping on chromosome 5 in human carcinomas. *Oncogene*. 12:97-102.
 - 12. Dracopoli NC, Houghton AN, Old LJ. (1985) Loss of polymorphic restriction fragments in malignant melanoma: implications for tumor heterogeneity. *Proc Natl Acad Sci US A*. 82:1470-4.
 - 13. Osborne RJ, Leech V. (1994) Polymerase chain reaction allelotyping of human ovarian cancer. *Br J Cancer*. 69:429-38.

15 Example 19: Glutaminyl-tRNA Synthetase (QARS) - Target Gene VARIA305

The human glutaminyl-tRNA synthetase gene is essential for cell survival

Glutaminyl-tRNA synthetase (QARS) catalyzes ATP dependent covalent attachment of glutamine to its cognate tRNA to form glutaminyl-tRNA. In the absence of glutaminyl-tRNA, protein synthesis is blocked in eucaryotic cells. Glutaminyl-tRNA synthetase is a single copy gene in man. Inhibition of its function is expected to be cell lethal, as shown for other tRNA synthetases (summarized above).

The human Glutaminyl-tRNA synthetase gene and mRNA have sequence variances.

A human cDNA encoding glutaminyl tRNA synthetase (QARS) was cloned by Lamour et al. (1) who expressed the cDNA in *E. coli* and demonstrated glutaminyl tRNA synthetase activity in bacterial extracts. The cloned human cDNA

(Genbank/EMBL accession number X76013) is 2437 nt in length and includes a 5' untranslated region of 5 nucleotides, an open reading frame of 2325 nucleotides encoding a 775 amino acid polypeptide, and a 3' untranslated region of 107 nt including 8 terminal nt of poly A.

5

We designed primers for amplification. The QARS cDNA was screened for sequence variance in 36 unrelated individuals using the single strand conformation polymorphism (SSCP) technique. One sequence variance was identified, a C vs. T transition at nucleotide 404, within the coding sequence. The published nucleotide at position 404 is C. The sequence variance does not affect the protein encoded.

10

The frequency of heterozygotes for the nucleotide 404 sequence variance is 11% in the 36 individuals tested (4/36). However three of 16 North American Whites are heterozygotes (19%), and one of four Japanese (25%) (see Target Gene Summary Table).

15

The QARS gene maps to 3p

20

The human QARS cDNA has been mapped to chromosome 3 by hybridization of a QARS probe to a panel of 25 human/rodent somatic cell hybrids (1). One somatic cell hybrid, not known to contain human chromosome 3, was positive for both the QARS probe and an ACY1 probe. ACY1 maps to human 3p21, suggesting QARS may also map in this area. We independently mapped QARS to chromosome 3 using primers from the 3' untranslated region to analyze the National Institute of General Medical Sciences (NIGMS) Human/Rodent Somatic Cell Hybrid Mapping Panel #2 by PCR (see page 704 of the NIGMS 1994/1995 Catalog of Cell Lines, available from the Coriell Cell Repository, Camden, NJ). The panel consists of 24 hybrid cell lines, each monochromosomal for one human chromosome. The QARS PCR product mapped to the hybrid containing human chromosome 3. All mapping techniques were conclusive

25

in showing only one locus for human QARS.

Chromosome band 3p21 is a site of frequent loss of heterozygosity. The short arm of chromosome 3 has been well studied in breast, cervical, esophageal, kidney, and lung cancers. These studies report frequent allele loss at 3p21, varying up to 100% in some studies of small cell lung cancer. Among other cancers LOH occurs in approximately 20-30% of breast cancers (2,3), 30-60% of cervical cancers (4,5), 10-40% of esophageal cancers (6,7), 45-80% of kidney cancers (8-10), 50-100% of nasopharyngeal cancers (11), 0-75% of squamous cell head and neck cancers (12), 30-60% of melanomas (13), 30-100% of non-small cell lung cancers (14-16) and 80-100% in small cell lung cancer (17-19). Other for which there are reports of LOH in at least 20% of cases include leukemia, pancreas cancer, sarcoma, testis cancer and ovarian cancer. Other cancer types, including bladder and lymphoma, have not been studied for LOH at 3p21.

15

20

25

10

5

References

- 1. Nomura, N., Nagase, T., Miyajima, N., et al. (1994) Prediction of the coding sequences of unidentified human genes. II. The coding sequences of 40 new genes (KIAA0041-KIAA0080) deduced by analysis of cDNA clones from human cell line KG-1. *DNA Research* 1:225-229.
- 2. Nichols, R.C., Blinder, J., Pai, S.I. et al. (1996) Assignment of two human autoantigen genes: isoleucyl tRNA synthetase locates to 9q21 and lysysl-tRNA synthetase locates to 16q23-24. *Genomics*: 210-213.
- 3. Cleton-Jansen AM, Moerland EW, Kuipers-Dijkshoom NJ, et al. (1994) At least two different regions are involved in allelic imbalance on chromosome arm 16q in breast cancer. *Genes Chromosom Cancer*. 9:101-7.
- 4. Dorion-Bonnet F, Mautalen S, Hostein I, Longy M. (1995) Allelic imbalance study of 16q in human primary breast carcinomas using microsatellite markers. *Genes Chromosomes Cancer*. 14:171-81.

25

- 5. Kashiwaba M, Tamura G, Suzuki Y, et al. (1995) Epithelial-cadherin gene is not mutated in ductal carcinomas of the breast. *Jpn J Cancer Res.* 86:1054-9.
- 6. O'Connell P, Pekkel V, Fuqua S, Osborne CK, Allred DC. (1994) Molecular genetic studies of early breast cancer evolution. *Breast Cancer Res Treat*. 32:5-12.
- 7. Sato T, Akiyama F, Sakamoto G, Kasumi F, Nakamura Y. (1991) Accumulation of genetic alterations and progression of primary breast cancer. *Cancer Res.* 51:5794-9.
- 8. Tsuda H, Callen DF, Fukutomi T, Nakamura Y, Hirohashi S. (1994) Allele loss on chromosome 16q24.2-qter occurs frequently in breast cancers irrespectively of differences in phenotype and extent of spread. *Cancer Res.* 54:513-7.
- 9. Fujimori M, Tokino T, Hino O, et al. (1991) Allelotype study of primary hepatocellular carcinoma. *Cancer Res.* 51:89-93.
 - 10. Fujimoto Y, Hampton LL, Wirth PJ, Wang NJ, Xie JP, Thorgeirsson SS. (1994) Alterations of tumor suppressor genes and allelic losses in human hepatocellular carcinomas in China [see comments]. *Cancer Res.* 54:281-5.
- 15 11. Tsuda H, Zhang WD, et al. (1990) Allele loss on chromosome 16 associated with progression of human hepatocellula carcinoma. Proc Natl Acad Sci USA. 87:6791-4.
 - 12. Tsuda H, Oda T, Sakamoto M, Hirohashi S. (1992) Different pattern of chromosomal allele loss in multiple hepatocellular carcinomas as evidence of their multifocal origin. *Cancer Res.* 52:1504-9.
- 13. Zhang WD, Hirohashi S, Tsuda H, et al. (1990) Frequent loss of heterozygosity on chromosomes 16 and 4 in human hepatocellular carcinoma. *Jpn J Cancer Res.* 81:108-11.
 - 14. Ookawa K, Sakamoto M, Hirohashi S, et al. (1993) Concordant p53 and DCC alterations and allelic losses on chromosomes 13q and 14q associated with liver metastases of colorectal carcinoma. *Int J Cancer*. 53:382-7.
 - 15. Genes, Chromosomes & Cancer 10: 177.
 - 16. Cancer Research 54: 2996.
 - 17. Gallion H.H., Powell D.E., Morrow J.K., et al. (1992) Molecular genetic changes in human epithelial ovarian malignancies [see comments]. *Gynecol Oncol.* 47:137-42.

- 18. Osborne RJ, Leech V. (1994) Polymerase chain reaction allelotyping of human ovarian cancer. *Br J Cancer*. 69:429-38.
- 19. Yang-Feng TL, Han H, Chen KC, et al. (1993) Allelic loss in ovarian cancer. *Int J Cancer*. 54:546-51.
- 20. British Journal of Urology 73: 390.
- 21. Okamoto A, Sameshima Y, Yamada Y, et al. (1991) Allelic loss on chromosome 17p and p53 mutations in endometrial carcinoma of the uterus. *Cancer Res.* 51:5632-5.

5

Example 20: Lysyl-tRNA Synthetase (KARS) - Target Gene VARIA303

Human Lysyl t-RNA synthase gene is essential

15

Lysyl-tRNA synthetase (KARS) catalyzes ATP dependent covalent attachment of lysine to its cognate tRNA to form lysyl-tRNA. In the absence of lysyl-tRNA, protein synthesis is blocked. Since lysyl-tRNA synthetase is a single copy gene in man, inhibition of its function is expected to be cell lethal. This has been shown for other tRNA synthetases (summarized above).

20

The human Lysyl-tRNA synthetase gene and mRNA have sequence variances

25

A human cDNA encoding a sequence similar to bacterial lysyl tRNA synthetases was cloned by Nomura et al. (GenBank/DDBJ submission D31890; see ref. 1) while sequencing random cDNAs. No biochemical studies of the protein encoded by this sequence have been reported. The 5' end of the sequence apparently begins in the coding region and the open reading frame continues for 1805 nucleotides, encoding 601 residues of a polypeptide (the full length of which has not been established), followed by a 3' untranslated region of 165 nucleotides.

PCT/US98/05419

232/116

We designed primers for amplification. The reported partial cDNA was screened for sequence variance in 36 unrelated individuals using the single strand conformation polymorphism (SSCP) technique as described in the methods section. Two sequence variances were identified, an A vs. G transition at nucleotide 89 and a G vs. C transversion at nucleotide 1798, both within the coding sequence. The published nucleotides are A and G, respectively. The nucleotide 1798 sequence variance alters the sense of the 599th codon (the third codon from the end of the coding sequence) to serine vs. threonine.

The frequency of KARS heterozygotes varies among the populations surveyed. The frequency of heterozygotes for the nucleotide 89 sequence variance is 19% in the 36 individuals tested. However all heterozygous individuals were either North American Whites (4/16; 25% heterozygotes), North American Blacks (1/4; 25%), or Hispanics (1/3; 33% heterozygotes). The frequency of heterozygotes for the nucleotide 1798 sequence variance is 6% in the 36 individuals tested. However all heterozygous individuals were North American Blacks (2/4; 50%) (see Target Gene Summary Table). Further study of these and other population groups will better establish the frequency of heterozygotes for these two sequence variances.

The KARS gene maps to 16q23-q24

WO 98/41648

5

10

15

20

25

The human KARS cDNA has been mapped to chromosome 16q22 by Nichols et al. (ref. 2) and by us. We designed primers to the 3' untranslated region of KARS and used PCR to analyze the National Institute of General Medical Sciences (NIGMS) Human/Rodent Somatic Cell Hybrid Mapping Panel #2 (see page 704 of the NIGMS 1994/1995 Catalog of Cell Lines, available from the Coriell Cell Repository, Camden, NJ). The panel consists of 24 hybrid cell lines, each monochromosomal for one human chromosome. The KARS PCR product mapped to the hybrid containing human chromosome 16. Similar results were obtained by Nichols et al., who mapped KARS

WO 98/41648

232/116

PCT/US98/05419

by analysis of the same NIGMS hybrid mapping panel, by PCR mapping in a chromosome 16 regional mapping panel and by fluorescence *in situ* hybridization to metaphase chromosomes. The *in situ* hybridization showed KARS maps to 16q23-q24. All mapping techniques were conclusive in showing only one locus for human KARS.

Loss of heterozygosity occurs frequently at 16q23-q24 in many cancer types. Loss of heterozygosity studies of chromosome 16q have principally focused on breast and liver cancers. In six detailed studies of breast cancer in the 16q23-q24 region LOH frequencies of 30-60% have been reported (refs 3-8). 16q22 LOH has ben reported in 35-65% of liver cancers (9-13), with the average around 45%. Studies of other cancer types report 16q22 LOH in 19% of colon cancers (14), 17-27% of esophageal cancers (15,16), 37% of ovarian cancers (new ref) (17-19), 18% of prostate cancers (20) and 23% of uterine cancers (21). Cancer types not yet investigated for LOH include kidney, leukemia and lymphoma, lung, melanoma, neuroblastoma, stomach and testis.

References

5

10

15

20

- 1. Nomura, N., Nagase, T., Miyajima, N., et al. (1994) Prediction of the coding sequences of unidentified human genes. II. The coding sequences of 40 new genes (KIAA0041-KIAA0080) deduced by analysis of cDNA clones from human cell line KG-1. *DNA Research* 1:225-229.
- 2. Nichols, R.C., Blinder, J., Pai, S.I. et al. (1996) Assignment of two human autoantigen genes: isoleucyl tRNA synthetase locates to 9q21 and lysysl-tRNA synthetase locates to 16q23-24. *Genomics*: 210-213.
- 3. Cleton-Jansen AM, Moerland EW, Kuipers-Dijkshoorn NJ, et al. (1994) At least two different regions are involved in allelic imbalance on chromosome arm 16q in breast cancer. Genes Chromosom Cancer. 9:101-7.
- 4. Dorion-Bonnet F, Mautalen S, Hostein I, Longy M. (1995) Allelic imbalance study

10

15

- of 16q in human primary breast carcinomas using microsatellite markers. Genes Chromosomes Cancer. 14:171-81.
- 5. Kashiwaba M, Tamura G, Suzuki Y, et al. (1995) Epithelial-cadherin gene is not mutated in ductal carcinomas of the breast. *Jpn J Cancer Res.* 86:1054-9.
- 6. O'Connell P, Pekkel V, Fuqua S, Osborne CK, Allred DC. (1994) Molecular genetic studies of early breast cancer evolution. *Breast Cancer Res Treat*. 32:5-12.
 - 7. Sato T, Akiyama F, Sakamoto G, Kasumi F, Nakamura Y. (1991) Accumulation of genetic alterations and progression of primary breast cancer. *Cancer Res.* 51:5794-9.
 - 8. Tsuda H, Callen DF, Fukutomi T, Nakamura Y, Hirohashi S. (1994) Allele loss on chromosome 16q24.2-qter occurs frequently in breast cancers irrespectively of differences in phenotype and extent of spread. *Cancer Res.* 54:513-7.
 - 9. Fujimori M, Tokino T, Hino O, et al. (1991) Allelotype study of primary hepatocellular carcinoma. *Cancer Res.* 51:89-93.
 - 10. Fujimoto Y, Hampton LL, Wirth PJ, Wang NJ, Xie JP, Thorgeirsson SS. (1994) Alterations of tumor suppressor genes and allelic losses in human hepatocellular carcinomas in China [see comments]. *Cancer Res.* 54:281-5.
 - 11. Tsuda H, Zhang WD, Shimosato Y, et al. (1990) Allele loss on chromosome 16 associated with progression of human hepatocellular carcinoma. *Proc Natl Acad Sci USA*. 87:6791-4.
- 12. Tsuda H, Oda T, Sakamoto M, Hirohashi S. (1992) Different pattern of chromosomal allele loss in multiple hepatocellular carcinomas as evidence of their multifocal origin. Cancer Res. 52:1504-9.
 - 13. Zhang WD, Hirohashi S, Tsuda H, et al. (1990) Frequent loss of heterozygosity on chromosomes 16 and 4 in human hepatocellular carcinoma. *Jpn J Cancer Res.* 81:108-11.
 - 14. Ookawa K, Sakamoto M, Hirohashi S, et al. (1993) Concordant p53 and DCC alterations and allelic losses on chromosomes 13q and 14q associated with liver metastases of colorectal carcinoma. *Int J Cancer*. 53:382-7.
 - 15. Genes, Chromosomes & Cancer 10: 177-

10

15

20

25

- 16. Cancer Research 54: 2996-
- 17. Gallion HH, Powell DE, Morrow JK, et al. (1992) Molecular genetic changes in human epithelial ovarian malignancies [see comments]. *Gynecol Oncol*. 47:137-42.
- 18. Osborne RJ, Leech V. (1994) Polymerase chain reaction allelotyping of human ovarian cancer. *Br J Cancer*. 69:429-38.
- 19. Yang-Feng TL, Han H, Chen KC, et al. (1993) Allelic loss in ovarian cancer. *Int J Cancer*. 54:546-51.
- 20. British Journal of Urology 73: 390-.
- 21. Okamoto A, Sameshima Y, Yamada Y, et al. (1991) Allelic loss on chromosome 17p and p53 mutations in human endometrial carcinoma of the uterus. *Cancer Res.* 51:5632-5.

Example 21: Ribosomal Protein S14 (RPS14) - Target Gene VARIA326

Ribosomal protein S14 is essential for cell growth

Human ribosomal protein S14 (RPS14) is one of ~80 unique protein constituents of the mammalian ribosome. Many of the protein subunits of ribosomes, the protein making machines of all cells, are highly conserved throughout prokaryotic and eukaryotic evolution (1). For example, human RPS14 protein is 100% amino acid identical to hamster S14 protein, 72% identical to yeast rp59 protein and 43% identical to *E. Coli* ribosomal protein S11 (2,3). Mammalian S14 and yeast rp59 are components of the 40S ribosomal subunit while *E. coli* S11 is part of the corresponding bacterial S30 subunit. Thus human RPS14 is a ribosomal component fixed early in evolution.

There are many antibiotics and eukaryotic cell poisons that act by inhibiting ribosome function (reviewed in ref. 4). One such drug is emetine, which inhibits protein translation by interacting with the eukaryotic RPS14 subunit to prevent elongation

10

15

20

25

factor dependent translocation of peptidyl-tRNAs bound to eukaryotic ribosomes in vitro (4).

Chinese hamster ovary (CHO) cell lines resistant to emetine have been shown to contain mutant RPS14 loci (also referred to as the EMTB locus) (5). Such lines have been used to investigate the effects of mutant RPS14 on ribosome function (5-8). Human-CHO cell hybrids are emetine-sensitive, indicating that the EMTB/RPS14 mutation is recessive in CHO cells. This is apparently because arrest of protein synthesis in half of ribosomes blocks translation of all polysomic mRNAs by blocking any functional ribosomes upstream of frozen mutant ribosomes. RPS14 appears to contribute to the structural integrity of the 40S subunit: 40S subunits containing mutant S14 protein are more easily dissociable in high ionic strength wash buffers (9). Ribosomal subunit genes are coordinately expressed in all cells and ribosomal proteins constitute a large fraction of the cell mass in all cell types.

The human RPS14 gene has sequence variances

Rhoads et al. reported the sequence of the human RPS14 gene and cDNA (3). The cDNA contains a 33 nucleotide 5' untranslated region, a 453 nt coding region and a 60 nt 3' untranslated region (including 12 nt of polyA). We undertook a systematic search for DNA sequence variance in the cDNA of RPS14 by analysing 36 unrelated individuals using the single strand conformation polymorphism technique. Primers were designed using the sequence of Rhoads et al. (GENBANK accession M13934, M13641; see ref. 3). SSCP analysis revealed 1 sequence variance, and subsequent DNA sequence analysis confirmed an A vs. G transition at nucleotide 183 of the coding sequence. (This change was noted as a difference between the cDNA and genomic sequences in ref. 3.)

As shown in the Target Summary Table, both alleles were detected in all major

populations surveyed, including North American Whites, North American Blacks, Hispanics, Chinese and Japanese.

The human RPS14 gene maps to chromosome 5q23-q33

5

Dana and Wasmuth (11) used Chinese hamster/human somatic cell hybrids to map the RPS14 gene (designated EMTB) to 5q23-5q35. Later Nakamichi et al. (12) placed the RPS14 gene on the segment 5q23-q33 using similar techniques.

10

15

25

Chromosome band 5q23-q33 is a site of frequent loss of heterozygosity. There have been many studies of LOH on 5q, particularly the 5q21-q22 region where the Adenomatous Polyposis Coli (APC) tumor suppressor gene lies. The most extensively studied cancers are those of the gastrointestinal tract, lung and ovary. The available data on the 5q23-q33 region just distal to APC (where RPS14 lies), suggests that LOH occurs in this region at a frequency of ~30% in cervical cancer (13), 20-40% in colon cancer (14,15), 30-50% in ovarian cancer (16,17), 38% in stomach cancer (18) and 23% in testicular cancer (19). There is also evidence for LOH in head and neck, lung, and liver cancers.

20 References

- 1. Chambliss, G., Craven, G.R., Davies, J., et al., editors, <u>Ribosomes: Structure</u>, <u>Function and Genetics</u>, University Park Press, Baltimore, 1980.
- 2. Chen, I.-T., Dixit, A., |Rhoads, D.D. and D.J. Roufa (1986) Homologous ribosomal proteins in bacteria, yeast and humans. *Proc. Natl. Acad. Sci. U.S.A.* 83: 6907-6911.
- 3. Rhoads, D. D.; Dixit, A.; Roufa, D. J. (1986) Primary structure of human ribosomal protein S14 and the gene that encodes it. *Molec. Cell. Biol.* 6: 2774-2783.
- 4. Vazquez, D. (1979) Molecular Biology and Biophysics, vol. 30, Inhibitors of Protein Synthesis. Springer-Verlag, Berlin.

- 5. Wasmuth, J.J. (1985) Chinese hamster cell protein synthesis mutants. In Gottesman, M., ed. Molecular Cell Genetics, pp. 397-421.
- 6. Rhoads, D.D. and D.J. Roufa (1985) Emetine resistance in Chinese hamster cells: structures of wild-type and mutant ribosomal protein AS14 mRNAs. Mol. Cell Biol. 5: 1655-1659.
- 7. Madjar, J.J., Nielsen-Smith, K., Frahm, M. and D. Roufa (1982) Emetine resistance in Chinese hamster ovary cells is associated with an altered ribosomal protein S14 mRNA. *Proc. Natl. Acad. Sci. U.S.A.* 79: 1003-1007.
- 8. Dana, S. L., Chang, S. and J.J. Wasmuth (1985) Synthesis and incorporation of human ribosomal protein S14 into functional ribosomes in human-Chinese hamster cell hybrids containing human chromosome 5: human RPS14 gene is the structural gene for ribosomal protein S14. *Somat. Cell Molec. Genet.* 11: 625-631.
- 9. Madjar, J.-J., Frahm, M., McGill, S. and D.J. Roufa (1983) *Molec. Cell. Biol.* 3: 190-197.
- 15 10. Mount, S. (1982) A catalogue of splice junction sequences. *Nucleic Acids Research* 19: 459-472.
 - 11. Dana, S. and J.J. Wasmuth (1982) Selective linkage disruption in human-Chinese hamster cell hybrids: deletion mapping of the leuS, hexB, emtB, and chr genes on human chromosome 5. *Molec. Cell. Biol.* 2: 1220-1228.
- 12. Nakamichi, N. N.; Kao, F.-T.; Wasmuth, J.; Roufa, D. J. (1986) Ribosomal protein gene sequences map to human chromosomes 5, 8 and 17. *Somat. Cell. Molec. Genet.* 12: 225-236.
 - 13. Mitra AB, Murty VV, Li RG, Pratap M, Luthra UK, Chaganti RS. (1994) Allelotype analysis of cervical carcinoma. *Cancer Res.* 54:4481-7.
- 25 14. Japanese Journal of Cancer Research 82: 1003.
 - 15. Cunningham C, Dunlop MG, Wyllie AH, Bird CC. (1993) Deletion mapping in colorectal cancer of a putative tumor suppressor gene in 8p22-p21.3. *Oncogene*. 8:1391-6.
 - 16. British Journal of Cancer 69: 429.

WO 98/41648 PCT/US98/05419

243 232/116

17. Weitzel J.N., Patel J., Smith D.M., Goodman A., Safaii H., Ball H.G. (1994) Molecular genetic changes associated with ovarian cancer. *Gynecol. Oncol.* 55:245-52.

- 18. Genes, Chromosomes and Cancer 3: 468
- 19. Murty VV, Bosl GJ, Houldsworth J, et al. (1994) Allelic loss and somatic differentiation in human male germ cell tumors. *Oncogene*. 9:2245-51.

Example 22: Eukaryotic Initiation Factor 5A (eIF-5A) - Target Gene VARIA351

Initiation Factor 5A is essential for cell growth

Human Initiation Factor 5A (eIF-5A), formerly named Initiation Factor 4D, is an 18-kD protein which promotes formation of the first peptide bond in *in vitro* translation systems - hence the name 'initiation factor' (1,2); however, the full physiological role of eIF-5A is not understood. Inhibition of eIF 5A formation blocks proliferation in all tested cell types (3); the presence of functional eIF 5A has been shown to correlate with the onset of DNA replication (4) - perhaps due to eIF 5A dependent translation of mRNAs encoding proteins necessary for DNA replication (3), and eIF-5A is an essential co-factor for HIV-1 Rev protein (5).

20

25

5

10

15

eIF 5A is an unusual protein: one of its lysine residues (amino acid 50) is modified by transfer and hydroxylation of the butylamino-group from the polyamine spermidine to form hypusine, a post translational modification unique to eIF 5A. All of the biological activities of eIF 5A are abrogated in the absence of the hypusine modification, as demonstrated by pharmacological inhibition of hypusine formation in human cell lines (3) and by site directed mutagenesis of the modified lysine residue in the yeast enzyme (6). There are two enzymes responsible for hypusine formation, one of which, deoxyhypusyl hydroxylase, can be inhibited with the drug mimosine (3), providing a convenient pharmacological inhibitor of eFI 5A formation.

The genome of the yeast Saccharomyces cerevisiae encodes two eIF 5A genes. Disruption of one (form A) slows growth, disruption of the other (form B) arrests growth and strains with both forms disrupted are non-viable (6). The yeast A form substitutes for human eIF 5A in the mammalian methionyl-puromycin synthesis assay (6), while the human gene complements eIF 5A disrupted yeast (7). eIF 5A is a highly conserved protein, with counterparts in archeae, bacteria and eukaryotes. The yeast proteins are ~63% identical to the human protein (6).

The human eIF 5A gene and mRNA have sequence variances

10

15

5

Smit-McBride, et al. reported the sequence of a human cDNA encoding eIF-5A (8) and Koettnitz et al. (8) later reported the sequence of the active eIF 5A gene, which contains three introns (GenBank accession U17969). A composite sequence made from the cDNA and genomic versions is 1309 nucleotides long and contains a 5' untranslated region of 145 nucleotides, a 462 nt coding region and a 702 nt 3' untranslated region (see annotated sequence). We undertook a systematic search for DNA sequence variance in the cDNA of eIF 5A by analysing 36 unrelated individuals using the single strand conformation polymorphism technique. Primers were designed for amplification. SSCP analysis revealed 2 sequence variances, and subsequent DNA sequence analysis confirmed an A vs. G transition at nucleotide 623 and a T vs. C transition at nucleotide 1012, both in the 3' untranslated sequence.

20

25

Neither sequence variance affects the protein coding sequence, however nucleotide 623 is one nucleotide away from a splice acceptor site at position 622, and could therefore be targeted by an oligonucleotide intended to abrogate splicing in an allele specific manner. The second exonic nucleotide (+2 position) of a splice acceptor site is not highly conserved, nonetheless the A vs. G transition at nucleotide 623 may affect the mechanics of splicing.

15

20

25

As shown in the Target Summary Table, both alleles were detected in all major populations surveyed, including North American Whites, North American Blacks, Hispanics, Arabs, Indians and Japanese, except only the nucleotide 1012 variance was detected in the four Chinese surveyed. The overall frequency of heterozygotes was 37% for the nucleotide 623 sequence variance and 52% for the nucleotide 1012 sequence variance.

The human eIF 5A gene maps to chromosome 17p13-p12

Steinkasserer et al. (1995) mapped the eIF 5A gene to 17p13-p12 by fluorescence *in situ* hybridization (9). Three eIF 5A pseudogenes were mapped to 10q23, 17q25 and 19q13.

Chromosome band 17p13-p12 is a site of frequent loss of heterozygosity. There have been many studies of LOH on 17p, particularly the 17p13 region where the p53 tumor suppressor gene maps. Virtually all cancer types have been surveyed for LOH in this area, with particularly extensive studies of breast, colon, ovarian, and stomach cancers. These studies report LOH in approximately 40-60% of breast cancers (10-18), 50-70% of colon cancers (19-25), 25-75% of ovarian cancers (26-30), 20-60% of stomach cancers (31-34), 20-50% of brain cancers (35,36), 45-70% of esophageal cancers (37), 35-65% of non-small cell lung cancers (38,39) and 100% of small cell lung cancers, 15-50% of cervical cancers, 30-80% of head and neck cancers, 20-60% of liver cancers, over 50% of sarcomas and 10-30% of a variety of other cancer types.

References

- 1. Wolff, E.C., Park, M.H. and J.E. Folk (1990) Journal of Biological Chemistry 265: 4793-4799.
- 2. Park, M.H., Wolff, E.C. and J.E. Folk (1993) Hypusine: its post-translational formation in eukaryotic translation factor 5A and its potential role in cellular

- regulation. Biofactors 4: 95-104.
- 3. Hanauske-Abel, H.M., Park, M.-H., Hanauske, A.-R., et al. (1994) Inhibition of the G1-S transition of the cell cycle by inhibitors of deoxyhypusine hydroxylation. *Biochimica et Biophysica Acta* 1221: 115-124.
- 4. Hanauske-Abel, H.M., Slowinska, B., Zagulska, S., et al. (1995) Detection of a subset of polysomal mRNAs associated with modulation of hypusine formation at the G1-S boundary. Proposal of a role for eIF 5A in onset of DNA replication. *FEBS Lett.* 366: 92-98.
 - 5. Ruhl, M., Himmelspach, M., Bahr, G.M., et al. (1993) Eukaryotic initiation factor 5A is a cellular target of the HIV-1 Rev activation domain mediating trans-activation. J. Cell Biol. 123:1309-1320.
 - 6. Schnier, J., Schwelberger, H.G., Smit-McBride, Z, et al. (1991) Translation initiation factor 5A and its hypusine modification are essential for cell viability in the yeast Saccharomyces Cerevisiae. *Molecular and Cellular Biology* 11: 3105-3114.
- 7. Koettnitz, K., Wohl, T., Kappel, B., Lottspeich, F., Hauber, J. and D. Bevec (1995) Identification of a new member of the human eIF-5A gene family. *Gene* 159: 283-284.
 - 8. Smit-McBride, Z., Dever, T.E., Hershey, J.W.B., et al. (1989) Sequence determination and cDNA cloning of eukaryotic initiation factor 4D, the hypusine containing protein. Journal of Biological Chemistry 264: 1578-1583.
 - 9. Steinkasserer, A.; Jones, T.; Sheer, D.; Koettnitz, K.; Hauber, J. and D. Bevec (1995) The eukaryotic cofactor for the human immunodeficiency virus type 1 (HIV-1) rev protein, eIF-5A, maps to chromosome 17p12-p13: three eIF-5A pseudogenes map to 10q23.3, 17q25, and 19q13.2. *Genomics* 25: 749-752.
- 10. Cornelis RS, van Vliet M, Vos CB, et al. (1994) Evidence for a gene on 17p13.3, distal to TP53, as a target for allele loss in breast tumors without p53 mutations.

 *Cancer Res. 54:4200-6.**
 - 11. Lindblom A, Skoog L, Rotstein S, Werelius B, Larsson C, Nordenskjold M. (1993) Loss of heterozygosity in familial breast carcinomas. *Cancer Res.* 53:4356-61.

15

20

- 12. Sato T, Akiyama F, Sakamoto G, Kasumi F, Nakamura Y. (1991) Accumulation of genetic alterations and progression of primary breast cancer. *Cancer Res.* 51:5794-9.
- 13. Singh S, Simon M, Meybohm I, et al. (1993) Human breast cancer: frequent p53 allele loss and protein overexpression. *Hum Genet*. 90:635-40.
- 14. Thorlacius S, Borresen AL, et al. (1993) Somatic p53 mutations in human breast carcinomas in an Icelandic population: a prognostic factor. *Cancer Res.* 53:1637-41.
- 15. Tsuda H, Hirohashi S. (1994) Association among p53 gene mutation, nuclear accumulation of the p53 protein and aggressive phenotypes in breast cancer. *Int J Cancer*. 57:498-503.
- 16. Watatani M, Nagayama K, Imanishi Y, et al. (1993) Genetic alterations on chromosome 17 in human breast cancer: relationships to clinical features and DNA ploidy. *Breast Cancer Res Treat*. 28:231-9.
 - 17. Chen LC, Neubauer A, Kurisu W, et al. (1991) Loss of heterozygosity on the short arm of chromosome 17 is associated with high proliferative capacity and DNA aneuploidy in primary human breast cancer. *Proc Natl Acad Sci U S A*. 88:3847-51.
 - 18. Sato T, Akiyama F, Sakamoto G, Kasumi F, Nakamura Y. (1991) Accumulation of genetic alterations and progression of primary breast cancer. *Cancer Res.* 51:5794-9.
 - 19. Burmer GC, Rabinovitch PS, Haggitt RC, et al. (1992) Neoplastic progression in ulcerative colitis: histology, DNA content, and loss of a p53 allele [see comments]. *Gastroenterology*. 103:1602-10.
 - 20. Cunningham C, Dunlop MG, Wyllie AH, Bird CC. (1993) Deletion mapping in colorectal cancer of a putative tumor suppressor gene in 8p22-p21. *Oncogene*. 8:1391-6
 - 21. Kikuchi-Yanoshita R, Konishi M, Ito S, et al. (1992) Genetic changes of both p53 alleles associated with the conversion from colorectal adenoma to early carcinoma in familial adenomatous polyposis and non-familial adenomatous polyposis patients. *Cancer Res.* 52:3965-71.
 - 22. Yin J, Harpaz N, Tong Y, et al. (1993) p53 point mutations in dysplastic and cancerous ulcerative colitis lesions. *Gastroenterology*. 104:1633-9.

- 23. Iacopetta B, DiGrandi S, Dix B, et al. (1994) Loss of heterozygosity of tumor suppressor gene loci in human colorectal carcinoma. *Eur J Cancer*. 5:664-70.
- 24. Law DJ, Olschwang S, Monpezat JP, et al. (1988) Concerted nonsyntenic allelic loss in human colorectal carcinoma. *Science*. 241:961-5.
- 5 25. Lothe RA, Nakamura Y, Woodward S, Gedde DT, Jr., White R. (1988) VNTR (variable number of tandem repeats) markers show loss of chromosome 17p sequences in human colorectal carcinomas. Cytogenet Cell Genet. 48:167-9.
 - 26. Foulkes WD, Stamp GW, Afzal S, et al. (1995) MDM2 overexpression is rare in ovarian carcinoma irrespective of TP53 mutation status. *Br J Cancer*. 72:883-8.
- 27. Phillips NJ, Ziegler MR, Radford DM, et al. (1996) Allelic deletion on chromosome 17p13.3 in early ovarian cancer. *Cancer Res.* 56:606-11.
 - 28. Foulkes WD, Black DM, Stamp GW, Solomon E, Trowsdale J. (1993) Very frequent loss of heterozygosity throughout chromosome 17 in sporadic ovarian carcinoma. *Int J Cancer*. 54:220-5.
- 29. Gallion HH, Powell DE, Morrow JK, et al. (1992) Molecular genetic changes in human epithelial ovarian malignancies [see comments]. *Gynecol Oncol*. 47:137-42.
 30. Phillips N. Ziegler M. Saha B. Xynos F. (1993) Allelic loss on chromosome 17 in
 - 30. Phillips N, Ziegler M, Saha B, Xynos F. (1993) Allelic loss on chromosome 17 in human ovarian cancer. *Int J Cancer*. 54:85-91.
 - 31. Seruca R, David L, Castedo S, Veiga I, Borresen AL, Sobrinho-Simoes M. (1994) p53 alterations in gastric carcinoma: a study of 56 primary tumors and 204 nodal metastases. *Cancer Genet Cytogenet*. 75:45-50.
 - 32. Kim CJ, Kim WH, Kim CW, Lee JB, Lee CK, Kim YL. (1995) Detection of 17p loss in gastric carcinoma using polymerase chain reaction. *Lab Invest*. 72:232-6.
 - 33. Ranzani GN, Renault B, Pellegata NS, et al. (1993) Loss of heterozygosity and Kras gene mutations in gastric cancer. *Hum Genet*. 92:244-9.
 - 34. Sano T, Tsujino T, Yoshida K, et al. (1991) Frequent loss of heterozygosity on chromosomes 1q, 5q, and 17p in human gastric carcinomas. *Cancer Res.* 51:2926-31.
 - 35. Frankel RH, Bayona W, Koslow M, Newcomb EW. (1992) p53 mutations in human malignant gliomas: comparison of loss of heterozygosity with mutation

25

frequency. Cancer Res. 52:1427-33.

- 36. Hermanson M, Funa K, Koopmann J, et al. (1996) Association of loss of heterozygosity on chromosome 17p with high platelet-derived growth factor alpha receptor expression in human malignant gliomas. *Cancer Res.* 56:164-71.
- 37. Aoki T, Mori T, Du X, Nisihira T, Matsubara T, Nakamura Y. (1994) Allelotype study of esophageal carcinoma. *Genes Chromosomes Cancer*. 10:177-82.
- 38. Tsuchiya E, Nakamura Y, Weng SY, et al. (1992) Allelotype of non-small cell lung carcinoma--comparison between loss of heterozygosity in squamous cell carcinoma and adenocarcinoma. *Cancer Res.* 52:2478-81.
- 39. Hiyama K, Ishioka S, Shirotani Y, et al. (1995) Alterations in telomeric repeat length in lung cancer are associated with loss of heterozygosity in p53 and Rb. Oncogene. 10:937-44.

Example 23: Replication Protein A, 32 kDa Subunit (RPA32) - Target Gene VARIA402

The human RPA32 gene encodes a protein essential for cell survival

Replication Protein A (RPA; also known as Replication Factor A, Activator 1, Single Strand Binding Protein or SSB) is a heterotrimeric protein which participates in DNA replication, homologous recombination and nucleotide excision repair (1-3). The evidence that RPA is an essential protein comes from *in vitro* and *in vivo* data.

DNA replication is essential for cell proliferation, as discussed above for RPA70.

The best studied function of RPA32 is in DNA replication. Because of the complexity of DNA replication in higher eukaryotic genomes, the small genome of the papovavirus SV40 has been used as a model system to study DNA replication in human cell extracts. In the 1980s several research groups

WO 98/41648

chromosomes as templates (4-8). An effort to identify the minimal set of factors required for DNA replication led to the discovery of RPA. Subsequent work proved that each of the three subunits of RPA is essential for DNA replication (9,10). This was proved in several ways, including by using antibodies to various constituents of the replication complex. Anti-RPA32 antibodies inhibit DNA replication, providing clear *in vitro* evidence for the essential function of this subunit of RPA in human DNA replication (10). The yeast *S. cerevisiae* has a trimeric replication protein A which is structurally and functionally homologous to the human protein. It consists of three subunits similar in size to the human subunits. All three yeast subunits have been disrupted and each disruption produces non-viable yeast (9).

The human RPA32 gene and mRNA are polymorphic.

15

20

25

10

5

The published cDNA for the 32 kD subunit of Replication Protein A is 1512 nucleotides long and includes a 5' untranslated segment of 77 nucleotides, followed by a protein coding region of 810 nucleotides and a 3' untranslated region of 625 nucleotides (10). We undertook a systematic search for DNA polymorphism by analysing the RPA32 cDNA from 36 unrelated individuals using the single strand conformation polymorphism technique (described in the methods section). Primers were designed using the sequence of Erdile et al. (GenBank accession J05249; see ref. 10). SSCP analysis revealed 2 variances, one of which was sequenced. Sequencing revealed a G vs. A transition at nucleotide 40 of the 5' untranslated region. Four of 36 individuals were heterozygotes, all of them Caucasians. Thus the allele frequency is 25% (4/16) in North American Whites, while no heterozygosity was detected in other populations (see Target Summary sheet).

The RPA32 gene maps to chromosome 1p35

The gene for RPA32 was mapped to chromosome band 1p35 by in situ hybridization, somatic cell hybrid analysis and yeast artificial chromosome mapping (11,12). Only one locus was detected by all methods.

5

Chromosome band 1p35 is a site of frequent loss of heterozygosity. The short arm of chromosome 1 is comparatively well investigated for allele loss, especially in breast and colon cancers. Studies of the 1p35 region show LOH in 15-40% of breast cancers (13,14), ~50% of gliomas (a brain cancer subtype) (15), 20-70% of colon cancers (16,17), ~50% of stomach cancers (18), ~20% of lung cancers (19) and 10-30% of ovarian cancers. High frequency LOH has been detected in several uncommon cancers such as pheochromocytoma (50-80%) and neuroblastoma (~50%).

References

15

10

1. Erdile, L. F., et al. Characterization of a cDNA encoding the 70-kDa single-stranded DNA-binding subunit of human replication protein A and the role of the protein in DNA replication. [published erratum appears in *J. Biol. Chem.* 1993 Jan 25;268(3):2268]. *J. Biol. Chem.* 266.18 (1991): 12090-8.

20

- 2. Jones, K. A., et al. A cellular DNA-binding protein that activates eukaryotic transcription and DNA replication. *Cell* 48.1 (1987): 79-89.
- 3. He, Z., et al. RPA involvement in the damage-recognition and incision steps of nucleotide excision repair. *Nature* 374.6522 (1995): 566-9.

- 4. Challberg, M. D., and T. J. Kelly. Eukaryotic DNA replication: viral and plasmid model systems. *Annu Rev Biochem* 51 (1982): 901-34.
- 5. Wold, M. S., et al. Identification of cellular proteins required for simian virus 40 DNA replication. *Journal Biological Chemistry* 264.5 (1989): 2801-9.
- 6. Kelly, T. J. DNA replication in mammalian cells: insights from the SV40 model system. *Harvey Lecture* 85 (1989): 173-88.

15

- 7. Hurwitz, J., Dean, F.B., Kwong, A.D and S.-H. Lee (1990) *Journal of Biological Chemistry* 265: 18043-18046.
- 8. Stillman, B. (1992) Initiation of chromosome replication in eukaryotic cells. *Harvey Lecture* 88: 115-40.
- 9. Brill, S.J. and B. Stillman (1991) Replication factor-A from Saccharomyces cerevisiae is encoded by three essential genes coordinately expressed at S phase. *Genes and Development* 5: 589-1600.
- 10. Erdile, L. F., M. S. Wold, and T. J. Kelly. The primary structure of the 32-kDa subunit of human replication protein A. <u>J Biol Chem</u> 265.6 (1990): 3177-82.
- 11. Ozawa, K., Dean, F., et al. (1993) Mapping of the 70 kDa 34kDa and 11kDa subunit genes of the human multimeric single-stranded DNA binding protein (hSSB/RPA) to chromosome bands 17p13, 1p35-p36.1 and 7p21-p22. *Cell Struct Funct* 18: 221-230.
 - 12. Umbricht, C. B., et al. High-resolution genomic mapping of the three human replication protein A genes (RPA1, RPA2, and RPA3). Genomics 20.2 (1994): 249-57.
 - 13. Bieche I, Champeme MH, Matifas F, Cropp CS, et al. (1993) Two distinct regions involved in 1p deletion in human primary breast cancer. *Cancer Res.* 53:1990-4.
 - 14. Borg A, Zhang QX, Olsson H, Wenngren E. (1992) Chromosome 1 alterations in breast cancer: allelic loss on 1p and 1q is related to lymphogenic metastases and poor prognosis. *Genes Chromosomes & Cancer*. 5:311-20.
 - 15. Reifenberger, J., Reifenberger, G., Liu, L., et al. (1994) Molecular genetic analysis of oligodendroglial tumors shows preferential allelic deletions on 19q and 1p. American Journal of Pathology 145: 1175-1190.
- 25 16. (1990) Cancer Research 50: 7232.
 - 17.Lothe RA, Nakamura Y, Woodward S, Gedde DT, Jr., White R. (1988) VNTR (variable number of tandem repeats) markers show loss of chromosome 17p sequences in human colorectal carcinomas. *Cytogenet Cell Genet*. 48:167-9.
 - 18. Ezaki, T., Yanagisawa, A., Ohta, K., et al. (1996) Deletion mapping on

PCT/US98/05419

232/116

chromosome 1p in well-differentiated gastric cancer. British Journal of Cancer 73: 424-428.

19. Hiyama K, Ishioka S, et al. (1995) Alterations in telomeric repeat length in lung cancer are associated with loss of heterozygosity in p53 and Rb. *Oncogene*. 10:937-44.

5

Example 24: Replication Protein A, 70 kD subunit (RPA70) - Target Gene VARIA401

10

The human RPA70 gene encodes a protein essential for cell survival

Replication Protein A (also known as Replication Factor A, Activator or Single Strand Binding protein [SSB]) is a heterotrimeric protein which participates in DNA replication, homologous recombination and nucleotide excision repair (1-3). The evidence that RPA is an essential protein comes from *in vitro*, *in vivo* and evolutionary data.

15

20

DNA replication is essential for cell proliferation, and a variety of antiproliferative drugs act, at least in part, by inhibiting DNA replication. Such drugs include nucleotide analogs that block DNA polymerases, such as 2',3' dideoxy NTPs and 3' deoxy ATP (cordycepin); inhibitors that bind to or modify DNA such as intercalating agents, DNA crosslinking drugs or alkylating agents, and inhibitors that bind to polymerases and replication proteins such as topoisomerase inhibitors like the epipodophyllotoxins, which prevent DNA unwinding necessary for replication (and transcription) and antibiotics which bind to polymerases such as arythydrazino-pyrimidines.

25

The best studied function of RPA70 is in DNA replication. Because of the complexity of DNA replication in higher eukaryotic genomes, the small genome of the papovavirus SV40 has been used as a model system to study DNA replication in human cell extracts. In the 1980s several research groups

WO 98/41648

254

232/116

developed cell free systems to study DNA replication using SV40 chromosomes as templates (4-8). These studies, in seeking to identify the minimal set of factors required for DNA replication, led to the discovery of replication protein A. Subsequent work proved that each of the three subunits of RPA is essential for DNA replications. This was proved in several ways, including by using antibodies to various constituents of the replication complex. These antibodies are effectively inhibitors of RPA70. Anti-RPA70 antibody mediated abrogation of DNA replication provides clear in vitro evidence for the essential function of RPA70 in human DNA replication (10). The yeast S. cerevisiae has a trimeric replication protein A which is structurally and functionally homologous to the human protein. It consists of three subunits similar in size to the human subunits. The yeast 70 kDa subunit is 31% identical and 75% similar (including conserved amino acids) to its human counterpart (1). All three yeast subunits have been disrupted and each disruption produces non-viable yeast. The yeast 70 kD protein is also a single stranded DNA binding protein.

Single stranded DNA binding proteins (SSBs) are required for DNA replication in a wide variety of organisms, including bacteriophage, bacteria and some DNA viruses of higher eukaryotes. Recently the crystal structure of the DNA binding domain of human RPA was solved and found to be remarkably similar in three dimensional shape to the bacteriophage single stranded DNA binding proteins Pf3 and gene V from f1 phage.

The human RPA70 gene, mRNA and protein have sequence variances

25

5

10

15

20

The published cDNA for the 70 kD subunit of Replication Protein A is 2393 nucleotides long and includes a 5' untranslated segment of 69 nucleotides, followed by a protein coding region of 1848 nucleotides and a 3' untranslated region of 476 nucleotides (1). We undertook a systematic search for DNA polymorphism by

. . .

WO 98/41648

5

10

15

20

25

255 232/116

PCT/US98/05419

analyzing the RPA70 cDNA from 36 unrelated individuals using the single strand conformation polymorphism technique (described in the methods section). Primers were designed using the sequence of Erdile et al. (GenBank accession M63488; see ref. 1). SSCP analysis revealed 5 variances, and subsequent DNA sequence analysis of those variances led to identification of four additional variances. SSCP revealed the variances at nucleotides 81 (G vs. A), 1120 (A vs. G), 1674 (T vs. C), 2050 (T vs. C) and 2297, where an insertion/deletion variance of one C nucleotide was observed (8 vs. 9 C's in a row). In the course of sequencing around the nucleotide 2297 polymorphism an additional variance was detected at nucleotide 2341 (A vs. G). Also, while sequencing additional Swedish individuals around nucleotide 1120 two new variances were observed at nucleotides 1124 and 125 (both C vs. T). Finally, in three individuals sequenced for the 2050 variance we noted a difference from the published sequence at nucleotide 2046: we detect 3 T's while the published clone shows just two. This difference may represent another insertion/deletion polymorphism. Five of the nine detected variances are in the coding sequence while four are in the 3' untranslated region.

The frequency of heterozygotes for the five SSCP positive variances ranged from 25-42% among the 36 individuals tested. The small number of individuals genotyped for the other four variances precludes definitive assessment of heterozygosity rates. Some of the polymorphisms appear to occur more commonly in certain racial or ethnic groups (see Target Summary sheet for details). For example, only one of the variances (nt 1674) was detected in Japanese individuals. In general, higher levels of polymorphism were detected in North American Whites than in other groups. The nucleotide 1120 polymorphism, for instance, was heterozygous in 9/36 individuals overall (25%), but in 8/16 North American Whites (50%).

The RPA70 cDNA encodes a 616 amino acid protein. The nucleotide 1120 and 1124 variances result in amino acid substitutions at residues 351 and 352, the former an alanine-threonine exchange (approximately 50% of caucasians are heterozygotes) and

WO 98/41648

PCT/US98/05419

the latter a serine-phenylalanine exchange (rare in the populations tested). In the recently published crystal structure of the DNA binding segment of RPA70 (amino acids 181-422) it is possible to place residue 351 in the second of two tandemly arrayed DNA binding domains (domain B; see ref. 10). Domain B extends from residue I305 to N402, thus the variant residue 351 is in the middle. The published structure is a cocrystal of RPA70 amino acids 181-422 complexed to octadeoxycytosine. Several RPA70 residues contact the oligonucleotide (Figure 4 of ref. 11), including amino acids K343 and T359, which lie 8 residues away from the polymorphism in either direction. Modeling the two variant forms of the protein using the atomic coordinates deposited in the Protein Data Bank (1JMC) should clarify the structural consequences of the alanine-threonine variance. Residue 351 lies in the center of a 50 amino acid segment of the protein that is relatively poorly conserved between yeast and man: 11 of the 50 residues are identical and 25 more are conservative substitutions. Towards the C terminus there is strong conservation: starting 25 residues C-terminal of the polymorphism, 27 of the next 37 residues are identical between yeast and man. Towards the N terminus there is ~30% conservation. Both yeast and human 70 kD RPA subunits contain putative C4-type zinc finger motifs at positions ~480-500.

The RPA70 gene maps to chromosome 17p13.3

20

5

10

15

The gene for RPA70 has been mapped to chromosome band 17p13.3 by in situ hybridization (12). Only one locus was detected.

25

Chromosome band 17p13.3 is a site of frequent loss of heterozygosity. RPA70 lies just telomeric to the TP53 tumor suppressor gene which is located in cytogenetic band 17p13.1. This region of chromosome 17 is extremely well investigated for allele loss. In general, studies report LOH in approximately 40-60% of breast cancers (13-21), 50-70% of colon cancers (22-28), 25-75% of ovarian cancers (29-33), 20-60% of stomach cancers (34-37), 20-50% of brain cancers (38,39), 45-70% of esophageal cancers (40),

232/116

35-65% of non-small cell lung cancers (41,42) and 100% of small cell lung cancers, 15-50% of cervical cancers, 30-80% of head and neck cancers, 20-60% of liver cancers, over 50% of sarcomas and 10-30% of a variety of other cancer types.

Assays developed for RPA: Protein and DNA contacts

Human cDNAs encoding all 3 subunits (70, 34 and 11 kD) of RPA have been cloned and expressed in *E. coli* and in insect cells via baculovirus vectors. The bacterially expressed 70 kDa protein is indistinguishable from its purified human counterpart immunologically and in several functional assays (see Table below). There is good evidence that the 70 kD subunit of RPA interacts with a number of different molecules. A partial list would include the 34 and 11 kD subunits of RPA, DNA, the xeroderma pigmentosum damage recognition and endonuclease proteins XPA and XPG, and DNA polymerase a-primase. These experimentally proven contacts (and almost certainly others) may constrain the topology of the protein in ways that have implications for inhibitor design. In summary a broad array of assays exists to screen for small molecule inhibitors of RPA (possibly including modified nucleotides), that act via competitive, allosteric or protein-protein blocking mechanisms.

Table 4

20

5

10

15

Assays and reagents available for RPA inhibitor screening

RPA 70 kD, Assay Systems

Purified Purifi	ed Bacterial or
Human Protein	Baculovirus
	Protein

ASSAY

Immunoreactivity	
Single stranded DNA binding	
DNA Polymerase alpha	
primase	

X	X
X	X
Х	X

30

232/116

DNA strand exchange
Nucleotide excision repair
Support SV40 Replication

X	X
X	X
X	X

5 References

10

- 1. Erdile, L. F., et al. Characterization of a cDNA encoding the 70-kDa single-stranded DNA-binding subunit of human replication protein A and the role of the protein in DNA replication. [published erratum appears in *J. Biol. Chem.* 1993 Jan 25;268(3):2268]. *J. Biol. Chem.* 266.18 (1991): 12090-8.
- 2. Jones, K. A., et al. A cellular DNA-binding protein that activates eukaryotic transcription and DNA replication. *Cell* 48.1 (1987): 79-89.
- 3. He, Z., et al. RPA involvement in the damage-recognition and incision steps of nucleotide excision repair. *Nature* 374.6522 (1995): 566-9.
- 4. Challberg, M. D., and T. J. Kelly. Eukaryotic DNA replication: viral and plasmid model systems. *Annu Rev Biochem* 51 (1982): 901-34.
 - 5. Wold, M. S., et al. Identification of cellular proteins required for simian virus 40 DNA replication. *Journal Biological Chemistry* 264.5 (1989): 2801-9.
 - 6. Kelly, T. J. DNA replication in mammalian cells: insights from the SV40 model system. *Harvey Lecture* 85 (1989): 173-88.
 - 7. Hurwitz, J., Dean, F.B., Kwong, A.D and S.-H. Lee (1990) Journal of Biological Chemistry 265: 18043-18046.
 - 8. Stillman, B. (1992) Initiation of chromosome replication in eukaryotic cells. *Harvey Lecture* 88: 115-40.
- 9. Heyer, W. D., et al. An essential Saccharomyces cerevisiae single-stranded DNA binding protein is homologous to the large subunit of human RP-A. *EMBO Journal* 9.7 (1990): 2321-9.
 - 10. Erdile, L. F., M. S. Wold, and T. J. Kelly. The primary structure of the 32-kDa subunit of human replication protein A. <u>J Biol Chem</u> 265.6 (1990): 3177-82.
- 30 11. Bochkarev, A., Pfuetzner, R.A., Edwards, A.M. and L. Frappier (1997) Structure

10

25

of the single stranded DNA binding domain of replication protein A bound to DNA. *Nature* 385: 176-181.

- 12. Umbricht, C. B., et al. High-resolution genomic mapping of the three human replication protein A genes (RPA1, RPA2, and RPA3). <u>Genomics</u> 20.2 (1994): 249-57.
- 13. Cornelis RS, van Vliet M, Vos CB, et al. (1994) Evidence for a gene on 17p13.3, distal to TP53, as a target for allele loss in breast tumors without p53 mutations. *Cancer Res.* 54:4200-6.
- 14. Lindblom A, Skoog L, Rotstein S, Werelius B, Larsson C, Nordenskjold M. (1993) Loss of heterozygosity in familial breast carcinomas. *Cancer Res.* 53:4356-61.
- 15. Sato T, Akiyama F, Sakamoto G, Kasumi F, Nakamura Y. (1991) Accumulation of genetic alterations and progression of primary breast cancer. *Cancer Res.* 51:5794-9.
 16. Singh S, Simon M, Meybohm I, et al. (1993) Human breast cancer: frequent p53 allele loss and protein over expression. *Hum Genet.* 90:635-40.
- 17. Thorlacius S, Borresen AL, et al. (1993) Somatic p53 mutations in human breast carcinomas in an Icelandic population: a prognostic factor. *Cancer Res.* 53:1637-41.

 18. Tsuda H, Hirohashi S. (1994) Association among p53 gene mutation, nuclear accumulation of the p53 protein and aggressive phenotypes in breast cancer. *Int J Cancer*. 57:498-503.
- 20 19. Watatani M, Nagayama K, Imanishi Y, et al. (1993) Genetic alterations on chromosome 17 in human breast cancer: relationships to clinical features and DNA ploidy. Breast Cancer Res Treat. 28:231-9.
 - 20. Chen LC, Neubauer A, Kurisu W, et al. (1991) Loss of heterozygosity on the short arm of chromosome 17 is associated with high proliferative capacity and DNA aneuploidy in primary human breast cancer. *Proc Natl Acad Sci USA*. 88:3847-51.
 - 21. Sato T, Akiyama F, Sakamoto G, Kasumi F, Nakamura Y. (1991) Accumulation of genetic alterations and progression of primary breast cancer. *Cancer Res.* 51:5794-9. 22. Burmer GC, Rabinovitch PS, Haggitt RC, et al. (1992) Neoplastic progression in ulcerative colitis: histology, DNA content, and loss of a p53 allele [see comments].

Gastroenterology. 103:1602-10.

- 23. Cunningham C, Dunlop MG, Wyllie AH, Bird CC. (1993) Deletion mapping in colorectal cancer of a putative tumor suppressor gene in 8p22-p21.3. *Oncogene*.8:1391-6
- 24. Kikuchi-Yanoshita R, Konishi M, Ito S, et al. (1992) Genetic changes of both p53 alleles associated with the conversion from colorectal adenoma to early carcinoma in familial adenomatous polyposis and non-familial adenomatous polyposis patients.

 Cancer Res. 52:3965-71.
 - 25. Yin J, Harpaz N, Tong Y, et al. (1993) p53 point mutations in dysplastic and cancerous ulcerative colitis lesions. *Gastroenterology*. 104:1633-9.
 - 26. Iacopetta B, DiGrandi S, Dix B, et al. (1994) Loss of heterozygosity of tumour suppressor gene loci in human colorectal carcinoma. *Eur J Cancer*. 5:664-70.
 - 27. Law DJ, Olschwang S, Monpezat JP, et al. (1988) Concerted nonsyntenic allelic loss in human colorectal carcinoma. *Science*. 241:961-5.
- 28. Lothe RA, Nakamura Y, Woodward S, Gedde DT, Jr., White R. (1988) VNTR (variable number of tandem repeats) markers show loss of chromosome 17p sequences in human colorectal carcinomas. *Cytogenet Cell Genet.* 48:167-9.
 - 29. Foulkes WD, Stamp GW, Afzal S, et al. (1995) MDM2 over expression is rare in ovarian carcinoma irrespective of TP53 mutation status. *Br J Cancer*. 72:883-8.
- 30. Phillips NJ, Ziegler MR, Radford DM, et al. (1996) Allelic deletion on chromosome 17p13.3 in early ovarian cancer. *Cancer Res.* 56:606-11.
 - 31. Foulkes WD, Black DM, Stamp GW, Solomon E, Trowsdale J. (1993) Very frequent loss of heterozygosity throughout chromosome 17 in sporadic ovarian carcinoma. *Int J Cancer*. 54:220-5.
- 32. Gallion HH, Powell DE, Morrow JK, et al. (1992) Molecular genetic changes in human epithelial ovarian malignancies [see comments]. Gynecol Oncol. 47:137-42.
 - 33. Phillips N, Ziegler M, Saha B, Xynos F. (1993) Allelic loss on chromosome 17 in human ovarian cancer. *Int J Cancer*. 54:85-91.
 - 34. Seruca R, David L, Castedo S, Veiga I, Borresen AL, Sobrinho-Simoes M. (1994)

10

15

20

25

- p53 alterations in gastric carcinoma: a study of 56 primary tumors and 204 nodal metastases. *Cancer Genet Cytogenet*. 75:45-50.
- 35. Kim CJ, Kim WH, Kim CW, Lee JB, Lee CK, Kim YL. (1995) Detection of 17p loss in gastric carcinoma using polymerase chain reaction. *Lab Invest.* 72:232-6.
- 36. Ranzani GN, Renault B, Pellegata NS, et al. (1993) Loss of heterozygosity and Kras gene mutations in gastric cancer. *Hum Genet*. 92:244-9.
- 37. Sano T, Tsujino T, Yoshida K, et al. (1991) Frequent loss of heterozygosity on chromosomes 1q, 5q, and 17p in human gastric carcinomas. *Cancer Res.* 51:2926-31.
- 38. Frankel RH, Bayona W, Koslow M, Newcomb EW. (1992) p53 mutations in human malignant gliomas: comparison of loss of heterozygosity with mutation frequency. *Cancer Res.* 52:1427-33.
- 39. Hermanson M, Funa K, Koopmann J, et al. (1996) Association of loss of heterozygosity on chromosome 17p with high platelet-derived growth factor alpha receptor expression in human malignant gliomas. *Cancer Res.* 56:164-71.
- 40. Aoki T, Mori T, Du X, Nisihira T, Matsubara T, Nakamura Y. (1994) Allelotype study of esophageal carcinoma. *Genes Chromosomes Cancer*. 10:177-82.
 - 41. Tsuchiya E, Nakamura Y, Weng SY, et al. (1992) Allelotype of non-small cell lung carcinoma--comparison between loss of heterozygosity in squamous cell carcinoma and adenocarcinoma. *Cancer Res.* 52:2478-81.
- 42. Hiyama K, Ishioka S, et al. (1995) Alterations in telomeric repeat length in lung cancer are associated with loss of heterozygosity in p53 and Rb. *Oncogene*. 10:937-44.

Example 25: RNA Polymerase II, 220-kD subunit (RPOL2A) - Target Gene VARIA500

The human RPOL2A gene encodes a protein essential for cell survival

DNA-dependent RNA polymerase II (also known as RPB1 or POLR2A), a complex

10

15

20

25

multisubunit enzyme, is responsible for the transcription of mRNA from all protein coding genes.

RNA polymerases are found in all cellular organisms. The subunit structure of RNA polymerases is highly conserved in eukaryotes. RNA polymerase acts in concert with as many as 50 other proteins in gene transcription (reviewed in ref. 1). See refs. 2 and 3 for a review of basal transcription by RNA polymerase II and recent progress in identifying and purifying transcription

factors and cloning the genes that encode them.

Several subunits of *S. cerevisiae* RPOL2A have been disrupted, always resulting in non-viable yeast.

A variety of inhibitors of RNA polymerase are cytotoxic drugs, such as actinomycin D, which intercalates into double stranded DNA and blocks the movement of RNA polymerase; rifampicin binds the b subunit of *E. coli* RNA polymerase and blocks initiation of transcription. The best studied specific inhibitor of eukaryotic RPOL2A, however, is the potent mushroom toxin - amanitin, a cyclic octapeptide which binds with high affinity (Kd ~10-9 M) to RPOL2A. Several mutations conferring resistance to a-amanitin have been characterized and they all map to the RPOL2A protein coding sequence. Recently a-amanitin binding has been shown to trigger specific degradation of RPOL2A (4).

Damage to actively transcribed DNA is preferentially repaired by the transcription-coupled repair (TCR) system. TCR requires RNA pol II, but the mechanism by which repair enzymes preferentially recognize and repair DNA lesions on PolB II-transcribed genes is incompletely understood.

The human RPOL2A gene and mRNA have sequence variances

Wintzerith et al. and later Mita et al. cloned and sequenced the complete human gene

PCT/US98/05419

232/116

WO 98/41648

5

10

15

20

25

for RPOL2A (5, 6); the deduced amino acid sequences are identical. The RPOL2A gene contains 29 exons and spans about 32 kb of DNA. The cDNA sequence we evaluated is 6732 nucleotides long (see Annotated RPOL2A Sequence) and contains a 5' untranslated region of 386 nucleotides, a 5910 nucleotide coding region specifying 1970 amino acids, and a 436 nucleotide 3' untranslated region (see annotated sequence). We undertook a systematic search for DNA sequence variance in the cDNA of RPOL2A by analyzing 36 unrelated individuals using the single strand conformation polymorphism technique. Primers were designed for amplification. SSCP analysis revealed 10 sequence variances, and subsequent DNA sequence analysis confirmed a G vs. A transition at nucleotide 857, a C vs. T transition at nucleotide 1260, a C vs. T transition at nucleotide 1346, a C vs. T transition at nucleotide 1544, a C vs. T transition at nucleotide 1847, a C vs. T transition at nucleotide 2678, a C vs. T transition at nucleotide 3059, a C vs. T transition at nucleotide 3827, a T vs. C transition at nucleotide 6466 and a T vs. C transition at nucleotide 6557. The former seven sequence variances are in coding sequence and the latter two are in the 3' untranslated sequence. Only one of the ten sequence variances alters the protein coding sequence: the nucleotide 1260 alleles encode arginine (common) or cysteine (rare) at amino acid 292. Only 2/36 individuals surveyed are heterozygotes (6%), however both are North American Whites (2/16 = 12.5%) so further investigation of this population is required. The prevalence of heterozygotes for the other sequence variances varies from 3% to 50%, with 6 sequence variances above 22% (see RPOL2A Target Summary Sheet). The 6 common sequence variances are widely prevalent among all or nearly all the tested populations.

The human RPOL2A gene maps to chromosome 17p13.105

The human RPOL2A gene was initially assigned to the distal portion of the short arm of chromosome 17 (17pter-p12) by *in situ* hybridization and Southern analysis of DNA from human/rodent somatic cell hybrids (7, 8). Subsequent somatic cell hybrid studies narrowed the assignment to 17p13.105-p12 [vanTuinen and Ledbetter (1987)], which

10

15

20

was later confirmed by in situ hybridization to 17p13 (9).

Chromosome band 17p13.1 is a site of frequent loss of heterozygosity There have been many studies of LOH on 17p, particularly the 17p13.1 region where the p53 tumor suppressor gene maps. Virtually all cancer types have been surveyed for LOH in this area, with particularly extensive studies of breast, colon, ovarian, and stomach cancers. These studies report LOH in approximately 40-60% of breast cancers (10-18), 50-70% of colon cancers (19-25), 25-75% of ovarian cancers (26-30), 20-60% of stomach cancers (31-34), 20-50% of brain cancers (35,36), 45-70% of esophageal cancers (37), 35-65% of non-small cell lung cancers (38,39) and 100% of small cell lung cancers, 15-50% of cervical cancers, 30-80% of head and neck cancers, 20-60% of liver cancers, over 50% of sarcomas and 10-30% of a variety of other cancer types.

References

- 1. Acker, J.; Mattei, M.-G.; Wintzerith, M.; Roeckel, N.; Depetris, D.; Vigneron, M.; Kedinger, C. (1994) Chromosomal localization of human RNA polymerase II subunit genes. *Genomics* 20: 496-499.
- 4. Buratowski, S. (1994) The basics of basal transcription by RNA polymerase II. *Cell* 77:1-3.
- 5. Cannizzaro, L. A., Emanuel, B. S., Cho, K. W. Y. and R. Weinmann (1986) The gene encoding the large subunit of human RNA polymerase II is located on the short arm of chromosome 17. *Am. J. Hum. Genet.* 38: 812-818.
- 8. Mita, K.; Tsuji, H.; Morimyo, M.; Takahashi, E.; Nenoi, M.; Ichimura, S.; Yamauchi, M.; Hongo, E., Hayashi, A. (1995) The human gene encoding the largest subunit of RNA polymerase II. *Gene* 159: 285-286.
 - 9. Pravtcheva, D.; Rabin, M.; Bartolomei, M.; Corden, J.; Ruddle, F. H. (1986) Chromosomal assignment of gene encoding the largest subunit of RNA polymerase II

WO 98/41648

5

15

20

PCT/US98/05419

232/116

265

in the mouse. Somat. Cell Molec. Genet. 12: 523-528.

- 13. Wintzerith, M., Acker, J., Vicaire, S., Vigneron, M. and C. Kedinger (1992) Complete sequence of the human RNA polymerase II largest subunit. *Nucleic Acids Res.* 20: 910.
- 10. Cornelis RS, van Vliet M, Vos CB, et al. (1994) Evidence for a gene on 17p13.3, distal to TP53, as a target for allele loss in breast tumors without p53 mutations. Cancer Res. 54:4200-6.
 - 11. Lindblom A, Skoog L, Rotstein S, Werelius B, Larsson C, Nordenskjold M. (1993) Loss of heterozygosity in familial breast carcinomas. *Cancer Res.* 53:4356-61.
- 12. Sato T, Akiyama F, Sakamoto G, Kasumi F, Nakamura Y. (1991) Accumulation of genetic alterations and progression of primary breast cancer. *Cancer Res.* 51:5794-9.
 13. Singh S, Simon M, Meybohm I, et al. (1993) Human breast cancer: frequent p53
 - allele loss and protein over expression. *Hum Genet*. 90:635-40.

 14. Thorlacius S, Borresen AL, et al. (1993) Somatic p53 mutations in human breast carcinomas in an Icelandic population: a prognostic factor. *Cancer Res.* 53:1637-41.
 - 15. Tsuda H, Hirohashi S. (1994) Association among p53 gene mutation, nuclear accumulation of the p53 protein and aggressive phenotypes in breast cancer. *Int J Cancer*. 57:498-503.
 - 16. Watatani M, Nagayama K, Imanishi Y, et al. (1993) Genetic alterations on chromosome 17 in human breast cancer: relationships to clinical features and DNA ploidy. *Breast Cancer Res Treat*. 28:231-9.
 - 17. Chen LC, Neubauer A, Kurisu W, et al. (1991) Loss of heterozygosity on the short arm of chromosome 17 is associated with high proliferative capacity and DNA aneuploidy in primary human breast cancer. *Proc Natl Acad Sci USA*. 88:3847-51.
- 18. Sato T, Akiyama F, Sakamoto G, Kasumi F, Nakamura Y. (1991) Accumulation of genetic alterations and progression of primary breast cancer. *Cancer Res.* 51:5794-9.
 19. Burmer GC, Rabinovitch PS, Haggitt RC, et al. (1992) Neoplastic progression in ulcerative colitis: histology, DNA content, and loss of a p53 allele [see comments]. *Gastroenterology*. 103:1602-10.

WO 98/41648

5

15

20

25

266 232/116

20. Cunningham C, Dunlop MG, Wyllie AH, Bird CC. (1993) Deletion mapping in colorectal cancer of a putative tumour suppressor gene in 8p22-p21.3. *Oncogene*. 8:1391-6

- 21. Kikuchi-Yanoshita R, Konishi M, Ito S, et al. (1992) Genetic changes of both p53 alleles associated with the conversion from colorectal adenoma to early carcinoma in familial adenomatous polyposis and non-familial adenomatous polyposis patients. *Cancer Res.* 52:3965-71.
- 22. Yin J, Harpaz N, Tong Y, et al. (1993) p53 point mutations in dysplastic and cancerous ulcerative colitis lesions. *Gastroenterology*. 104:1633-9.
- 23. Iacopetta B, DiGrandi S, Dix B, et al. (1994) Loss of heterozygosity of tumour suppressor gene loci in human colorectal carcinoma. *Eur J Cancer*. 5:664-70.
 - 24. Law DJ, Olschwang S, Monpezat JP, et al. (1988) Concerted nonsyntenic allelic loss in human colorectal carcinoma. *Science*. 241:961-5.
 - 25. Lothe RA, Nakamura Y, Woodward S, Gedde DT, Jr., White R. (1988) VNTR (variable number of tandem repeats) markers show loss of chromosome 17p sequences in human colorectal carcinomas. *Cytogenet Cell Genet.* 48:167-9.
 - 26. Foulkes WD, Stamp GW, Afzal S, et al. (1995) MDM2 over expression is rare in ovarian carcinoma irrespective of TP53 mutation status. *Br J Cancer*. 72:883-8.
 - 27. Phillips NJ, Ziegler MR, Radford DM, et al. (1996) Allelic deletion on chromosome 17p13.3 in early ovarian cancer. *Cancer Res.* 56:606-11.
 - 28. Foulkes WD, Black DM, Stamp GW, Solomon E, Trowsdale J. (1993) Very frequent loss of heterozygosity throughout chromosome 17 in sporadic ovarian carcinoma. *Int J Cancer*. 54:220-5.
 - 29. Gallion HH, Powell DE, Morrow JK, et al. (1992) Molecular genetic changes in human epithelial ovarian malignancies [see comments]. *Gynecol Oncol.* 47:137-42. 30. Phillips N, Ziegler M, Saha B, Xynos F. (1993) Allelic loss on chromosome 17 in human ovarian cancer. *Int J Cancer.* 54:85-91.
 - 31. Seruca R, David L, Castedo S, Veiga I, Borresen AL, Sobrinho-Simoes M. (1994) p53 alterations in gastric carcinoma: a study of 56 primary tumors and 204 nodal

10

15

20

25

metastases. Cancer Genet Cytogenet. 75:45-50.

- 32. Kim CJ, Kim WH, Kim CW, Lee JB, Lee CK, Kim YL. (1995) Detection of 17p loss in gastric carcinoma using polymerase chain reaction. *Lab Invest.* 72:232-6.
- 33. Ranzani GN, Renault B, Pellegata NS, et al. (1993) Loss of heterozygosity and K-ras gene mutations in gastric cancer. *Hum Genet*. 92:244-9.
- 34. Sano T, Tsujino T, Yoshida K, et al. (1991) Frequent loss of heterozygosity on chromosomes 1q, 5q, and 17p in human gastric carcinomas. *Cancer Res.* 51:2926-31.
- 35. Frankel RH, Bayona W, Koslow M, Newcomb EW. (1992) p53 mutations in human malignant gliomas: comparison of loss of heterozygosity with mutation frequency. *Cancer Res.* 52:1427-33.
- 36. Hermanson M, Funa K, Koopmann J, et al. (1996) Association of loss of heterozygosity on chromosome 17p with high platelet-derived growth factor alpha receptor expression in human malignant gliomas. *Cancer Res.* 56:164-71.
- 37. Aoki T, Mori T, Du X, Nisihira T, Matsubara T, Nakamura Y. (1994) Allelotype study of esophageal carcinoma. *Genes Chromosomes Cancer*. 10:177-82.
- 38. Tsuchiya E, Nakamura Y, Weng SY, et al. (1992) Allelotype of non-small cell lung carcinoma--comparison between loss of heterozygosity in squamous cell carcinoma and adenocarcinoma. *Cancer Res.* 52:2478-81.
- 39. Hiyama K, Ishioka S, Shirotani Y, et al. (1995) Alterations in telomeric repeat length in lung cancer are associated with loss of heterozygosity in p53 and Rb. Oncogene. 10:937-44.

Example 26: TATA Associated Factor 30 kD subunit (TAF2H) - Target Gene VARIA 520

The human TAF2H gene encodes a component of the transcriptional apparatus

Transcription initiation by RNA polymerase II requires the assembly of a complex of

10

15

20

25

PCT/US98/05419

basic transcription factors which include TFIIA, TFIIB, TFIID, TFIIE, TFIIF, TFIIG/TFIIJ and TFIIH/BTF2 into a preinitiation complex (1,2). TFIID is the first factor to contact the promotor, and subsequent assembly of the transcription complex is dependent on TFIID binding. TFIID is a 700-750 kD multiprotein complex which includes TATA binding protein (TBP) and between eight and 13 TBP-associated factors (TAFs) ranging from 250 to 17 kDa. The TAFs have been shown necessary to reconstitute activation of transcription in vitro, leading to the hypothesis that some TAFs link transcription activation domains to the basal transcription complex. The TFIID complex also supports transcription from TATA-less promoters, while TBP fails to do so. Therefore TAFs may also contribute to formation of stable initiation complexes by interacting directly with DNA (2). Conditional temperature sensitive Chinese hamster mutants of another TAF, TAFII250, were detected because, at the non-permissive temperature, DNA synthesis was inhibited leading to arrest of cell division at the G1 phase (3,4). Transfection of a human TAFII250 gene relieved the block at the non-permissive temperature. Thus an essential role has been proven for TAFs in mammalian cells.

A gene (TAF2H) encoding the 30 kDa human TAF protein (TAFII30) was cloned and its functional properties examined by Jacq, et al. (5). The protein was shown to be present in a subset of TFIID complexes and to mediate transcriptional activation by a specific region of the estrogen receptor. Estrogen mediated transcriptional activation could be abrogated by adding an antibody against TAFII30. TAFII30 was not required for basal transcription or for transcription activation by VP-16. It is likely that TAFII30 is required for transcriptional activation by a variety of other transactivating proteins, and is therefore essential for cell proliferation or cell survival.

A human TAF2H cDNA has been cloned and sequenced (5). It encodes a cDNA of 756 nucleotides including a 5' untranslated region of 17 nucleotides, a 657 nucleotide

The human TAF2H gene and mRNA have sequence variants

WO 98/41648 PCT/US98/05419

coding region specifying 218 amino acids, and an 82 nucleotide 3' untranslated region (GenBank accession U13991; see annotated TAF2H cDNA sequence). (Note that the numbering of the sequence in ref. 5 differs slightly from that in the GenBank accession.) We undertook a systematic search for DNA variance in the cDNA of TAF2H by analysing 36 unrelated individuals using the single strand conformation polymorphism technique Primers were designed for amplification. SSCP analysis revealed 1 polymorphism, and subsequent DNA sequence analysis confirmed a G vs. A transition at nucleotide 554 (nt 556 of the sequence in ref. 3) of the coding sequence. This variance does not alter the protein coding sequence. Eight of 36 individuals surveyed are heterozygotes (22%). The variance occurs in North American Whites (3/16 = 19%), North American Blacks (2/4) and Hispanics (3/3).

5

10

15

20

25

The human TAF2H gene maps to chromosome 11p15.5-p15.2 The human TAF2H cDNA has been mapped to 11p15.5-p15.2 by fluorescent in situ hybridization (6). There appears to be a single TAF2H locus. Chromosome band 11p15-p14 is a site of frequent loss of heterozygosity

There have been many studies of LOH on 11p, particularly the 11p15 and 11p13 segments where the Beckwith-Weidemann syndrome and WT1 genes reside. As a result there are many studies of LOH in 11p15.5, particularly focusing on breast, cervix, kidney, liver, lung, ovarian, stomach and testicular cancers. These studies show that the 11p15.5 band of chromosome 11 is frequently reduced to one copy (7-24). For example, LOH occurs in approximately 13-33% of breast cancers (7-9), 14-42% of cervical cancers (10), 0-50% of liver cancers (11,12), 0-80% of lung cancers (13-15), 18-54% of ovarian cancers (14,15), 0-71% of stomach cancers (18) and 0-50% of testicular cancers (19,20). Other studies show that 11p15.5 LOH may also be frequent in bladder cancer (21), esophageal cancer (22), some leukemias (23) and sarcomas (24). Many deletions in the 11p15.5 region span relatively short chromosomal segments (2 - 10 megabases; see ref. 13).

References

10

15

20

- 1. Buratowski, S.(1994) The basics of basal transcription by RNA polymerase II. *Cell* 77: 1-3.
- 5 2. Tjian, R. and T. Maniatis (1994) Transcriptional activation: a complex puzzle with few easy pieces. *Cell* 77: 5-8.
 - 3. Sekiguchi, T., Miyata, T. and T. Nishimoto (1988) Molecular cloning of the cDNA of human X chromosomal gene (CCG1) which complements the temperature sensitive G(1) mutants, tsBN462 and ts13, of the BHK cell line. *EMBO Journal* 7: 1683-1687.
 - 4. Hisatake, K., Hasegawa, S., Takada, R., et al. (1993) The p250 subunit of native TATA box-binding factor TFIID is the cell-cycle regulatory protein CCG1. *Nature* 362: 172-181.
 - 5. Jacq, X., Brou, C., Lutz, Y., Davidson, I., Chambon, P. and L. Tora (1994) Human TAFII30 is present in a distinct TFIID complex and is required for transcriptional activation by the estrogen receptor. *Cell* 79: 107-117.
 - 6. Scheer, E., Mattei, M.G., Jacq, X., Chambon, P. and L. Tora (1995) Organization and chromosomal localization of the gene (TAF2H) encoding the human TBP-associated factor II 30 (TAFII30). *Genomics* 29: 269-272.
 - 7. Ali, I., Lidereau, R., Theilley, C. and R. Callahan (1987) Reduction to homozygosity of genes on chromosome 11 in human breast neoplasia. *Science* 238:185-8.
 - 8. Winqvist, R., Mannermaa, A., Alavaikko, M., Blanco, G., Taskinen, P.J., Kiviniemi, H., Newsham, I. and W. Cavenee (1993) Refinement of regional loss of heterozygosity for chromosome 11p15.5 in human breast tumors. *Cancer Research* 53: 4486-4488.
 - 9. Carter, S.L., Negrini, M., Baffa, R., et al. (1994) Loss of heterozygosity at 11q22-q23 in breast cancer. *Cancer Research* 54:6270-4.
 - 10. Mitra, A.B., Murty, V.V.V.S., Li, R.G., et al. (1994) Allelotype analysis of cervical carcinoma. *Cancer Research* 54:4481.

10

15

20

25

- 11. Fujimori, M., Tokino, T., Hino, O., et al. (1991) Allelotype study of primary heptocellular carcinoma. *Cancer Research* 51: 89-93.
- 12. Wang, H.P. and C.E. Rogler (1988) Deletions in human chromosome arms 11p and 13q in primary hepatocellular carcinomas. *Cytogenetics and Cell Genetics* 48:72-78.
- 13. Bepler, G. and Garcia-Blanco, M.A. (1994) Three Tumor Suppressor Regions on Chromosome 11p Identified by High Resolution Deletion Mapping in Human Non-Small Cell Lung Cancer. *Proc. Natl. Acad. Sci. U.S.A.* 91:5513-7.
- 14. Iizuka, M., Sugiyama, Y., Shiraishi, M., Jones, C. and T. Sekiya (1995) Allelic losses in human chromosome 11 in lung cancers. *Genes, Chromosomes & Cancer* 13:40-46.
- 15. Weston, A., Willey, J.C., Modali, R., et al. (1989) Differential DNA sequence deletions from chromosomes 3, 11, 13 and 17 in squamous cell carcinoma, large-cell carcinoma and adenocarcinoma of the human lung. *Proc. Natl. Acad. Sci. U.S.A.* 86:5099-5103.
- 16. Kiechle-Schwartz, M., Bauknecht, T., Wienker, T., et al. (1993) Loss of Constitutional Heterozygosity on Chromosome 11p in Human Ovarian Cancer. Cancer 72:2423-32.
- 17. Viel, A., Giannini, F., Tumiotti, L., Sopracordevole, F., Visentin, M.C. and M. Boiocchi (1992) Chromosomal localization of two putative 11p oncosuppressor genes involved in human ovarian tumors *British Journal of Cancer* 66: 1030-1036.
- 18. Baffa, R., Negrini, M., Mandes, B., et al. (1996) Loss of heterozygosity for chromosome 11 in adenocarcinoma of the stomach. *Cancer Research* 56: 268-72.
- 19. Lothe, R.A., Hastie, N., Heimdal, K., et al. (1993) Frequent loss of 1p13 and 11p15 loci in male germ cell tumors. *Genes, Chromosomes & Cancer* 7: 96-101.
- 20. Smith, R.C., and Rukstalis, D.B. (1995) Frequent Loss of Heterozygosity at 11p Loci in Testicular Cancer. *The Journal of Urology* 153: 1684-7.
- 21. Shaw, M.E. and Knowles, M.A. (1995) Deletion Mapping of Chromosome 11 in Carcinoma of the Bladder. *Genes, Chromosomes & Cancer* 13: 1-8.

- 22. Shibagaki, I., Shimada, Y., Wagata, T., Ikenaga, M., Imamura, M. and K. Ishizaki (1994) Allelotype analysis of esophageal squamous cell carcinoma. *Cancer Research* 54: 2996-3000.
- 23. Ahuja, H.G., Foti, A., Zhou, D.J. and M.J. Cline (1990) Analysis of proto-oncogenes in acute myeloid leukemia: loss of heterozygosity for the Ha-ras gene. *Blood* 75: 819-822.

Example 27 - cDNA synthesis

10

15

20

5

In order to analyze an essential gene for sequence variances, it is generally useful to have a cDNA(s) containing the coding sequence for further sequencing or amplification purposes. cDNAs for some genes are available, however, in some cases it is useful to synthesize the cDNA de novo. Methods for obtaining cDNA are known to those skilled in the art, as are methods for sequencing or amplifying the cDNA or portions thereof. An example of a useful cDNA production protocol is provided below, however, as recognized by those skilled in the art, other specific protocols can also be used.

cDNA Production

- Make sure that all tubes and pipette tips are RNase-free. (Bake them overnight at 100oC in the vacuum oven to make them RNase-free.)
- Add the following to a RNase-free 0.2 ml micro-amp tube and mix gently:
- 25 24 ul water (DEPC treated)
 - 12 ul RNA (lug/ul)
 - 12 ul random hexamers(50 ng/ul)
 - 2 Heat the mixture to 70oC for ten minutes.
 - 3 Incubate on ice for 1 minute.

232/116

4 Add the following:

16 ul 5 X Synthesis Buffer

8 ul 0.1 M DTT

4 ul 10 mM dNTP mix (10 mM each dNTP)

4 ul SuperScript RT II enzyme

Pipette gently to mix.

- 5 Incubate at 42oC for 50 minutes.
- 6 Heat to 70oC for ten minutes to kill the enzyme, then place it on ice.
- Add 160 ul of water to the reaction so that the final volume is 240 ul.
 - 8 Use PCR to check the quality of the cDNA. Use primer pairs that will give a
 - ~800 base pair long piece. See "PCR Optimization" for the PCR protocol.

The following chart shows the reagent amounts for a 20 ul reaction, a 80 ul reaction, and a batch of 39 (which makes enough mix for 36) reactions:

	20 ul X 1 tube	80 ul X 1 tube	80ul X 39 tubes	
water	6 ul	24 ul	936	water
RNA	3 ul	12 ul		RNA
random hexamers	3 ul	12 ul	468	random hexamers
synthesis buffer	4 ul	16 ul	624	synthesis buffer
0.1 M DTT	2 ul	8 ul	312	0.1 M DTT
10mM dNTP	l ul	4 ul	156	10mM dNTP
SSRT	l ul	4 ul	156	SSRT

30

5

10

15

20

25

Example 28 - Variance detection by SSCP

10

15

20

25

This example describes the SSCP technique as used for the identification of sequence variances of the exemplary genes, which were then sequenced to confirm the specific base variances. One common technique currently employed in the identification of such single nucleotide differences is the single strand conformation polymorphism (SSCP) method. (originally described in Orita, et al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the Polymerase Chain Reaction, Genomics, 5:874-879 (1989)) Also employed are restriction fragment length polymorphism (RFLP), heteroduplex analysis, ligase chain reaction (LCR), denaturing gradient gel electrophoresis (DGGE) (Myers, Maniatis, and Lerman, Methods Enzymol., 155:501-527 (1987)) or direct nucleotide sequencing. A review of polymorphism detection techniques, including SSCP, is provided in Grompe, 1993, Nature Genetics 5:111-117, which includes a comparison of the commonly used methods.

The SSCP method reveals the presence of sequence variation between individuals as shifts in electrophoretic mobility, but does not show the sequence itself. Direct sequencing of DNAs with altered mobility in the SSCP assay identifies the precise nucleic acid sequence differences among the various alleles. From the nucleic acid sequence data, the amino acid sequence can be determined. One example of the use of this technique is in Pelletier et al., Cell, 67:437-447 (1991). The single strand conformation polymorphism methodology is effective for scanning essential genes for sequence variants. It remains the standard technique in human genetics for variance detection, with numerous studies of its efficacy (>90%) and schemes for improved throughput. The SSCP method has been shown to be quite sensitive in the detection of single base changes, for example as shown in Ravnik-Glava et al., 1994, Human Mol. Genet. 3:801-807 (human cystic fibrosis gene) and Glava & Dean, 1993, Human Mutation 2:404-414 (mouse -globin gene).

A flow chart of the SSCP method as used to identify essential gene sequence variants is shown in Fig. 2 (SSCP OVERVIEW). The method involves the steps of 1) PCR

232/116

amplifying a portion of an essential gene cDNA of known sequence (labeled products), 2) selecting restriction enzymes which will produce fragments approximately 100-400 bases in length for 3 independent digestions of the PCR products, 3) heat denaturing the digestion products, 4) running single strand digestion products on non-denaturing gels, 5) identifying bands having different mobilities when compared between individuals, thereby identifying potential sequence variants, 6) sequence at least the region around the potential sequence variance, that region being identified by comparison of the expected fragment sizes resulting from the digestions, 7) record the specific location and base identity of the confirmed sequence variant, 8) calculate the percent occurrence of each sequence variance for the gene as found for the sample of the population. The method is further described in Example 2.

5

10

15

20

25

Single strand conformation polymorphism screening is a widely used technique for identifying an discriminating DNA fragments which differ from each other by as little as a single nucleotide. As originally developed by Orita (supra), the technique was used on genomic DNA, however the same group showed that the technique works very well on PCR amplified DNA as well. In the last 8 years the technique has been used in hundreds of published papers, and the modifications of the technique have been described in dozens of papers. The enduring popularity of the technique is due to (1) a high degree of sensitivity to single base differences (>90%) (2) a high degree of selectivity, measured as a low frequency of false positives, and (3) technical ease. SSCP is almost always used together with DNA sequencing because SSCP does not directly provide the sequence basis of differential fragment mobility. The basic steps of the SSCP procedure are described below and summarized in Fig. 2 in flow chart form.

Because the intent of our SSCP screening was to identify as many target gene variances as practically possible, we developed a protocol designed to look at a relatively large number of individuals (36) with a high degree of redundancy, so as to minimize both the false negative and false positive rates.

PCT/US98/05419

232/116

The 36 individuals examined are reasonably representative of most of the worlds major populations. The racial or geographic origin of the 36 cell lines is detailed in the Target Summary Tables (Figure 5). All cell lines are EBV immortalized lyphoblastoid cells obtained from the Coriell Cell Repository (Camden, NJ), which includes the racial/ethnic/geographic background of cell line donors in its catalog. The cell lines were also selected for their rapid growth rates. In several cases a panel of cDNAs isolated from French Canadians was used instead, or in addition to, the Coriell panel.

276

WO 98/41648

5

10

15

20

25

SSCP was used to analyze cDNAs (rather than genomic DNAs) because in many cases the full genomic sequence of the target gene is not available, however, the technique is also applicable to genomic sequences. To produce cDNA requires RNA. Therefore each of the 36 cell lines was grown to mass culture and RNA was isolated using the acid/phenol protocol, sold in kit form as TRIAZOLTM by Life Technologies (Gaithersberg, MD). The unfractionated RNA was used to produce cDNA by the action of a modified Maloney Murine Leukemia Virus Reverse Transcriptase, purchased in kit form from Life Technologies (SUPERSCRIPT IITM kit). The reverse transcriptase was primed with random hexamer primers to initiate cDNA synthesis along the whole length of the RNAs. This proved useful later in obtaining good PCR products from the 5' ends of some genes.

Material for SSCP analysis was prepared by PCR amplification of the cDNA in the presence of one ³²P labeled dNTP (usually ³²P dCTP). Usually the concentration of nonradioactive dCTP was dropped from 200 uM (the standard concentration for all four dNTPs) to about 100 uM, and ³²P dCTP was added to a concentration of about 0.1-0.3 uM. This involved adding a 0.3-1 ul (3-10 uCi) of ³²P cCTP to a 10 ul PCR reaction. All radioactivity was purchased from DuPont/New England Nuclear.

The customary practice is to amplify about 200 base pair PCR products for SSCP, however, we found that it was preferable to amplify about 0.8-1.4 kb fragments and

PCT/US98/05419

232/116

WO 98/41648

5

10

15

20

25

then use several cocktails of restriction endonucleases to digest those into smaller fragments of about 0.1-0.4kb, aiming to have as many fragments as possible between .15 and .3 kb. The digestion strategy had the advantage that less PCR was required, reducing both time and costs. Also, we routinely performed three different digests on each sample (for all 36 cDNAs), and then ran each of the digests separately on SSCP gels. This had the effect of increasing the redundancy of our method, lessening both the false negative and false positive rates. For example: a site of variance might lie within 2 bases of the end of a fragment in one digest, and as a result not affect the conformation of that strand; the same variance, in a second or third digest, would likely lie in a location more prone to affect strand folding, and therefore be detected by SSCP.

After digestion, the radiolabeled PCR products were diluted 1:5 by adding formamide load buffer (80% formamide, 1X SSCP gel buffer) and then denatured by heating to 90%C for 10 minutes, and then allowed to renature by quickly chilling on ice. This procedure (both the dilution and the quick chilling) promotes intra- (rather than inter-) strand association and secondary structure formation. The secondary structure of the single strands influences their mobility on nondenaturing gels, presumably by influencing the number of collisions between the molecule and the gel matrix (i.e., gel sieving). Even single base differences consistently produce changes in intrastrand folding sufficient to register as mobility differences on SSCP.

The single strands were then resolved on two gels, one a 5.5% acrylamide, 0.5X TBE gel, the other an 8% acrylamide, 10% glycerol, 1X TTE gel. The use of two gels provides a greater opportunity to recognize mobility differences. Both glycerol and acrylamide concentration have been shown to influence SSCP performance. The gel apparatus we use (from Owl Scientific, MA) allows 108 samples to be loaded per gel. Since all 36 samples are routinely digested with three different endonuclease mixes there are 108 samples to be analyzed for each PCR product. By routinely analyzing three different digests under two gel conditions (effectively 6 conditions), and by

WO 98/41648

278

232/116

looking at both strands under all 6 conditions, we achieve a 12-fold sampling of each base pair of cDNA.

5

All of the sequence variances described in this disclosure were determined by DNA cycle sequencing of ³²P labeled PCR products using the femtomole DNA cycle sequencing kit from Promega (WI) and the instructions provided with the kit. Fragments were selected for DNA sequencing based on their behavior in the SSCP assay.

10

Example 29 - Variance detection by using T4 endonuclease VII mismatch cleavage method

15

The enzyme T4 endonuclease VII is derived from the bacteriophage T4. T4 endonuclease VII is used by the bacteriophage to cleave branched DNA intermediates which form during replication so the DNA can be processed and packaged. T4 endonuclease can also recognize and cleave heteroduplex DNA containing single base mismatches as well as deletions and insertions. This activity of the T4 endonuclease VII enzyme can be exploited to detect sequence variances present in the general population.

20

The following are the major steps involved in identifying sequence variations in a candidate gene by T4 endonuclease VII mismatch cleavage:

25

- Amplification by the polymerase chain reaction (PCR) of 400-600 bp regions
 of the candidate gene from a panel of DNA samples. The DNA samples can
 either be cDNA or genomic DNA and will represent some cross section of the
 world population.
- 2. Mixing of a fluorescently labeled probe DNA with the sample DNA. Heating

279 232/116

and cooling the mixtures causing heteroduplex formation between the probe DNA and the sample DNA.

- Addition of T4 endonuclease VII to the heteroduplex DNA samples. T4
 endonuclease will recognize and cleave at sequence variance mismatches
 formed in the heteroduplex DNA.
- 4. Electrophoresis of the cleaved fragments on an ABI sequencer to determine the site of cleavage.
- 5. Sequencing of a subset of PCR fragments identified by T4 endonuclease VI to contain variances to establish the specific base variation at that location.

A more detailed description of the procedure is as follows:

5

10

15

20

25

A candidate gene sequence is downloaded from an appropriate database. Primers for PCR amplification are designed which will result in the target sequence being divided into amplification products of between 400 and 600 bp. There will be a minimum of a 50 bp of overlap not including the primer sequences between the 5' and 3' ends of adjacent fragments to ensure the detection of variances which are located close to one of the primers.

Optimal PCR conditions for each of the primer pairs is determined experimentally. Parameters including but not limited to annealing temperature, pH, MgCl₂ concentration, and KCl concentration will be varied until conditions for optimal PCR amplification are established. The PCR conditions derived for each primer pair is then used to amplify a panel of DNA samples (cDNA or genomic DNA) which is chosen to best represent the various ethnic backgrounds of the world population or some designated subset of that population.

One of the DNA samples is chosen to be used as a probe. The same PCR conditions used to amplify the panel are used to amplify the probe DNA. However, a

280

232/116

flourescently labeled nucleotide is included in the deoxy-nucleotide mix so that a percentage of the incorporated nucleotides will be fluorescently labeled.

5

10

15

20

25

The labeled probe is mixed with the corresponding PCR products from each of the DNA samples and then heated and cooled rapidly. This allows the formation of heteroduplexes between the probe and the PCR fragments from each of the DNA samples. T4 endonuclease VII is added directly to these reactions and allowed to incubate for 30 min. at 37 C. 10 ul of the Formamide loading buffer is added directly to each of the samples and then denatured by heating and cooling. A portion of each of these samples is electrophoresed on an ABI 377 sequencer. If there is a sequence variance between the probe DNA and the sample DNA a mismatch will be present in the heteroduplex fragment formed. The enzyme T4 endonuclease VII will recognize the mismatch and cleave at the site of the mismatch. This will result in the appearance of two peaks corresponding to the two cleavage products when run on the ABI 377 sequencer.

Fragments identified as containing sequencing variances are subsequently sequenced using conventional methods to establish the exact location and sequence variance.

Example 30 - Identification of Sequence Variances by Informatics-based analysis of gene-sequence databases

In addition to and/or in conjunction with the molecular biology based approaches for identifying sequence variances in genes, particularly in essential genes, such sequence variances can be identified by analysis of public and/or private genetic sequence databases. Such information can be either genomic or cDNA sequence information.

The data base analysis process includes the following major steps:

WO 98/41648

1.

2.

capture of homologous sequences of a particular gene from data bases. It is
preferable to obtain a large number of independent sequences of a particular
gene

5

10

analysis of collected sequences of a particular gene to identify authentic sequence variances. This step involves the discrimination of authentic sequence variances, which are sequence variances which actually exist in the population, from sequencing errors and artifacts. It is expected that about 0.1-0.3% of the bases will occur as true variances, while the frequency of sequencing artifacts is expected to be 1-3%. This discrimination utilizes the expected frequencies of occurrence of specific types of nucleotide sequence changes. Such information includes the characteristic frequency of specific transitions and transversions and of the characteristic frequency of deletions and insertions in authentic variations. It uses the frequency of occurrence of known types of sequencing artifacts such as single base insertions or deletions adjacent to repeated C or G nucleotides. Additional information for such discrimination is provided if particular putative authentic variations are observed in multiple independently derived sequences of the gene.

15

20

25

An implementation of this sequence variance identification process utilizes a reference sequence of an essential gene. Preferably, the reference sequence is a high quality sequence, meaning that there is a low frequency of occurrence of sequencing errors or artifacts. The second step is the retrieval of allelic sequences of that essential gene from available databases such as the BLAST server, the UNIGENE database, or other such sequence database. Such allelic sequences need not be complete, but are preferably long enough to ensure that they are in fact allelic sequences. The third step involves alignment analysis to identify and tabulate sequence differences between the different available sequences. An algorithm for such analysis is the Smith-Waterman local alignment algorithm. Use of an algorithm of this type involves a series of pair-

10

15

20

25

wise alignments of each retrieved sequence with the reference sequence. The fourth step involves analysis of the observed sequence differences and assignment of a probability that each sequence difference represents an authentic variance. This analysis utilizes program filters which are combined in a weighted fashion to determine a final probability. Such program filters include comparison of the observed difference with common mutational changes and sequencing errors, a weighting of the reliability of a particular retrieved sequence based on the total number of differences observed, a weighting based on the location within a retrieved sequence where a change was observed and a significant weighting based on the observance of a particular difference in multiple independently derived retrieved sequences.

Using such an implementation, a database analysis with respect to a particular reference sequence produces a list of putative authentic sequence variances and a probability for each of those variances that the sequence difference is an authentic variance. As described above, the probability is obtained through the use of a series of weighted program filters and thus these filters are modified to produce optimal authentic variance discrimination.

Example 31 - Antiproliferative effects of variance specific inhibition of RPA70

This example describes experiments showing the practicality and utility of variance-specific inhibition of essential genes for cancer therapy. Specifically, this example describes in vitro experiments showing the design and production of variance-specific oligonucleotides for antisense inhibition of variant alleles of the essential Replication Protein A, 70 kDa subunit (RPA70) for inhibition of RPA70 mRNA, and the use of these oligonucleotides to inhibit cell proliferation and to reduce the number of cells in a variance-specific manner.

Variance-specific inhibition and cell killing with antisense oligonucleotides against

283 232/116

RPA70

5

10

15

20

25

These experiments with RPA70 illustrate the feasibility of each of the steps for development of a variance specific inhibitor:

Select candidate target gene essential for cell survival or proliferation. As described above, RPA is essential for replication in prokaryotic and eukaryotic cells, mitochondria, phage, viruses and in *in vitro* (SV40) replication systems. The protein is a heterotrimer required for loading DNA polymerase onto the DNA template during cell replication. The 70 kDa subunit, RPA70, is a single strand binding protein that mediates the interaction of RPA with DNA. Without this protein, the replication complex does not associate with DNA and the replication of DNA does not occur.

Confirm chromosome location and LOH frequency. RPA70 is encoded by a single gene locus on chromosome 17pl3.3, immediately adjacent to the p53 gene at 17p13.1. LOH involving chromosome band 17pl3.3 has been documented in 50-70% of colon, lung, breast, and ovarian cancers. LOH at this locus also occurs in other cancers. The inventor as confirmed LOH involving RPA 70 in breast, colon, lung and other cancers.

Identify common variances in the normal population. We have identified five common variances in the RPA70 gene (Figure 8). The most common occurs in 42% of the normal population. One variance alters the amino acid sequence and is present in 25% of the normal population (44% of Caucasians). This variance occurs within the active DNA binding domain (discussed below). These variances are described in the description above and in Fig. 1.

Demonstrate antiproliferative effects due to inhibition of candidate gene. The inventor has shown that inhibition of RPA70 in T24 bladder carcinoma cells with an antisense oligonucleotide reduces cell number. This effect is comparable to treatment of these cells with antisense oligonucleotide against *ras*, previously shown to have antitumor

284

232/116

effects in vitro and in vivo (Figure 9).

5

10

15

20

25

Design variance-specific inhibitor. Variance specific antisense oligonucleotides were designed to differentially inhibit the two variant forms of RPA70. Experiments were performed using tumor cell lines that are homozygous for each form of the target gene. Figure 10 shows inhibition of mRNA levels in Mia Paca II cells by the 13085 oligonucleotide which matches the variance in these cells. In contrast, in T24 cells (and A549 cells, see below) the 12781 oligonucleotide matches the target gene and inhibits mRNA levels. In both cell lines neither the control oligonucleotide differing by one base (13085 in T24 cells and 12781 in Mia Paca II cells) nor a random-sequence oligonucleotide control (13706) inhibit mRNA levels to the same extent as the matched oligonucleotide.

Figure 10 demonstrates that the RPA 70 mRNA can be specifically down regulated in an allele-specific manner. However, the 13085 oligomer used also has a small effect on the level of the unmatched RNA. In order to increase the discrimination we altered the structure of the targeting oligomer, 13085. The results are shown in Figure 11. By shortening the oligomer we retain its ability to down-regulate its matched target RNA (Mia Paca II cells, right half of Figure 11). Strikingly, however, this alteration dramatically altered the ability of this oligomer to down-regulate the mismatched variant RNA T24 cells, left half of Figure 11. The reciprocal regulation by oligomer 12781 was augmented by altering transfection conditions. These data suggest that even simple changes to the rudimentary "first generation" chemistry and transfection techniques can have significant effects in enhancing the ability of the oligomers to recognize and down regulate specific mRNAs.

Achieve variance-specific antiproliferative effects in cancer cells. Cell proliferation in each cell line, determined by BrdU incorporation, was suppressed to a greater degree by the matched oligonucleotide than by the controls differing by one base (Figure 12).

PCT/US98/05419

232/116

Cell proliferation in A549 cells was inhibited by oligomer 12781 to a greater degree than by oligomer 13085. Cell proliferation in Mia Paca 11 cells was inhibited more by oligomer 13085.

Additional studies were performed to characterize the antiproliferative effect in A549 cells (12781 genotype). A dose response curve demonstrates inhibition of BrdU incorporation by the matched oligonucleotide (12781) at concentrations 8-fold lower than the oligonucleotide with one base mismatch (13085) (Figure 13).

Cell survival was measured by staining cells with Sulforhodamine B dye 72 hours after treatment with oligonucleotides. Dose dependent reductions in cell number were observed in cells treated with the matched oligonucleotide (12781) but not with an oligonucleotide containing the one base mismatch (13085) (Figure 14). In contrast, in Mia Paca II cells, more cell killing was observed with the 13085 oligonucleotide than with the 12781 oligonucleotide (Figure 15). The oligonucleotides used in these studies have not been optimized for achieving allele-specific effects. Oligonucleotides using advanced chemistries can be utilized to optimize the potency and provide greater discrimination between variant targets at lower levels.

20

25

5

10

15

WO 98/41648

Example 32 - variance specific inhibition of essential genes

This example describes experiments showing the practicality and utility of variance-specific inhibition of essential genes for cancer therapy including RNA Pol II, and ribonucleotide reductase. Specifically, this example describes in vitro experiments showing the design and production of variance-specific oligonucleotides for antisense inhibition of variant alleles of the essential Ribonuclotide Reductase (RR), the design and production of variance-specific oligonucleotides against RR, and the use of these oligonucleotides to inhibit RR mRNA in a variance-specific manner.

10

15

20

25

Variance-specific inhibition of Ribonucleotide Reductase.

Ribonucleotide Reductase (RR) is an essential gene of nucleoside metabolism. Inhibitors of this function are known to be cell lethal. Two variances were discovered at position 2410 and 2419. Oligonucleotides were synthesized to a sequence spanning these two variations. In one case the oligomer targeted the GnnnnnnnnA variation (oligomer Varia 2410GA or RR2410GA) and in the other case the oligomer targeted the AnnnnnnnnG variant (oligomer Varia 2410AG or RR2410AG). In Mia Paca II cells which contain the GnnnnnnnA variance, the RR2410GA antisense oligomer dramatically knocked down the level of RR mRNA. However, the oligomer targeting the other variance, oligomer Varia 2410AG, had little to no effect on the level of mRNA (Figure 16). The reciprocal regulation was demonstrated in MDA-MB 468 cells which express the other variance, AnnnnnnnnG (Figure 17). In these cells Varia 2410AG dramatically lowered the level of RR mRNA. In contrast, Varia 2410GA had no effect on the level of mRNA. These data taken together, are another example of allele-specific targeting of gene expression. We are also determining the effect of down regulating RR gene expression on cellular growth.

Example 33 - variance specific inhibition of essential genes using advanced oligonucleotide chemistries.

This example describes experiments showing the practicality and utility of variance-specific inhibition of essential genes for cancer therapy. Specifically, this example describes in vitro experiments showing the design and production of variance-specific oligonucleotides for antisense inhibition of variant alleles of the essential Glutamyl/prolyl tRNA Synthetase (EPRS), the design and production of variance-specific oligonucleotides against EPRS, and the use of these oligonucleotides to inhibit EPRS mRNA in a variance-specific manner.

Glutamyl-prolyl-tRNA synthetase (EPRS) is an essential gene, required for the synthesis of both glutamic acid tRNA and proline tRNA. Without EPRS protein synthesis is blocked. Two variances were discovered in this gene at positions 2963 and 2969 in the cDNA. We have demonstrated variance-specific inhibition of this gene with antisense oligonucleotides exploiting several different types of chemistry.

The experiments described above with RPA70 and RR utilized phophorothioate chemistry. This chemistry was developed to achieve greater stability in vivo, and this compound ha been used in several successful clinical trials. Phosphorothioates, however have low affinity for the RNA target, and, consequently, relatively lower specificity. We have achieved improved variance-specific inhibition using alternative chemistries. Specifically, we have synthesized hybrid oligonucleotides that contain both phosphorothioate and nucleotides with higher affinities. These hybrids contain "wings" consisting of six nucleotides with a 2' sugar modification (ethoxy-methoxy radical at the 2' position) and either a phosphorothioate or phosphodiester backbone. Between the "wings" is a 8 nucleotide sequence of phosphorothioates that overlaps the variance. (In these constructs the 5' position of cytosine has been methylated.) As shown in Figure 18, variance specific inhibition is observed with the conventional phorphorothioates. Greater inhibition of target mRNA is observed using the hybrid chemistries at lower doses. Inhibition by the matched hybrid oligomer, 14977, occurs at approximately 50-100 nM. The effect is extremely oligomer-specific. The mismatched oligomer, 14971, has no effect on mRNA levels at concentrations as high as 400 nM (Figure 19).

25

5

10

15

20

Example 34 - in vivo cancer therapy using oligonucleotides

This example describes reported in vitro and in vivo data on the treatment of cancer in animal models using antisense oligonucleotides against c-raf, showing the expected

288

232/116

correlation between *in vitro* suppression of mRNA and cell proliferation with oligonucleotides, and *in vivo* anticancer activity.

5

10

15

20

25

In vitro evidence for inhibition of mRNA by antisense oligonucleotides and inhibition of cell proliferation is commonly used to predict *in vivo* effects on tumors. This is exemplified by the publication by Monia et al (Nature Medicine, Volume 2 Number 6, June 1996) who demonstrated anticancer effects using oligonucleotides against C-raf kinase. In vitro treatment of human tumor cells with appropriate phosphorothioate antisense oligomers led to specific inhibition of C-raf kinase gene expression and subsequent decrease in cellular proliferation, IC50=50-100nM. Administration of C-raf antisense oligomers to nude mice having a tumor burden derived from these cells significantly inhibited tumor growth *in vivo*, IC50= 0.06-0.6 mg/kg. Remarkably, the investigators were able to show that the anti-C-raf oligomers down-regulated the level of C-raf kinase mRNA *in vivo* by assaying mRNA levels in cells removed from the tumor.

Example 35 - in vivo cancer therapy by oligonucleotide inhibition of ras

This example describes reported in vivo data showing an anticancer effect using an allele-specific inhibitor for suppression of mutant H-ras. Schwab et al (Proc. Nat. Acad. Sci. USA 91:10460-464, Oct 1994) demonstrated antitumor effects of an antisense oligonucleotide specific for the mutant ras in animal models. In these experiments HBL100 cells were transformed with the RAS oncogene. In vitro studies demonstrated that the RAS mRNA could be specifically down-regulated by a nanoparticle conjugated phosphodiester antisense oligomer. Only the transforming RAS mRNA was targeted by the oligomer. The normal cellular RAS mRNA, differing by a single base, was not affected by the antisense oligomer. The decrease in RAS expression was associated with a decrease in the growth rate of the cells. The

232/116

transformed HBL100 cells were injected into nude mice to form tumors; following subcutaneous injection of nanoparticle-conjugated phosphodiester antisense oligomers, Schwab et al measured both a decrease in targeted tumor weight and volume. Specificity for tumor cell growth correlated well with the *in vitro* data having a 5-fold differential between antisense and control groups.

The authors of this paper are proceeding with clinical trial of these oligonucleotides for the treatment of cancer, demonstrating the potential clinical utility of these methods.

10

15

20

25

5

Example 36. Variance detection by DGGE

This example describes denaturing gradient gel electrophoresis (DGGE), a technique used for the identification of DNA sequence variances in genomic DNA, cDNA or in PCR products amplified from genomic DNA or cDNA. The DGGE method was originally described by Fischer and Lerman (Two Dimensional Electrophoretic Separation of Restriction Enzyme Fragments of DNA. Methods in Enzymology, vol. 68: 183-191, 1979; DNA Fragments Differing by Single Base-Pair Substitutions are Separated in Denaturing Gradient Gels: Correspondence with Melting Theory. Proc. Natl. Acad. Sci. U.S.A. 80:1579, 1983) and has been improved since then by many investigators. See, for example: Myers, et al., Mutation Detection by PCR, GC-Clamps, and Denaturing Gradient Gel Electrophoresis, pp. 71-88 in Erlich, H.A., editor: PCR Technology: Principles and Applications for DNA Amplification, Stockton Press, New York, 1989; Myers, et al., Detecting Changes in DNA: Ribonuclease Cleavage and Denaturing Gradient Gel Electrophoresis, in Davies, K.E., editor: Genomic Analysis: A Practical Approach, IRL Press Ltd., Oxford, 1988, pp. 95-139; E.S. Abrams and V.P. Stanton Jr., Use of Denaturing Gradient Gel Electrophoresis, pp. 71-104 in Lilley, D.M.J. and Dahlberg, J.E., editors: DNA Structures, Part B: Chemical and Electrophoretic Analysis of DNA, Methods in

290

232/116

Enzymology, volume 212, Academic Press, 1992; .) Descriptions of current applications of the technique can be found in

The basic principal of DGGE involves the creation of a gradient of denaturant in a gel, which is then used to resolve double stranded DNA (or RNA) fragments on the basis of conformational differences associated with strand melting. The denaturant can be chemical (as in DGGE, where a gradient of formamide and urea is typically used) or thermal (as in a related technique called thermal gradient gel electrophoresis, or TGGE, where a gradient of heat is used). To obtain conditions where double stranded DNA is close to melting, DGGE gels are immersed in a heated bath of electrophoresis buffer, while TGGE gels have a fixed concentration of chemical denaturant.

5

10

15

20

25

As a double stranded DNA molecule migrates through a DGGE gel from a low concetration of denaturant at the origin to higher concentrations of denaturant toward the end of the gel it eventually reaches a level of denaturant that will cause partial melting. (Some design of DNA molecules is often necessary to assure that the partial melting will occur as desired; see below.) The concentration of denaturant required to melt a given DNA segment is highly sensitive to sequence differences in the DNA, including changes as subtle as a single nucleotide substitution. Partially melted DNA fragments move through gels at a much slower rates than their fully duplex counterparts. Thus two DNA fragments differing at a single nucleotide can be distinguished on the basis of their gel position after an appropriate period of electrophoresis: the fragment with the more stable structure (resulting from, for example, a G:C base pair in place of an A:T pair) will travel further in the gel than its less stable counterpart, because it will encounter the concentration of gradient required to melt it (and consequently dramatically retard or nearly stop its movement) at a point further along in the gel.

The DGGE method reveals the presence of sequence variation between individuals as

10

15

20

25

shifts in electrophoretic mobility, but does not show the sequence itself. Direct sequencing of DNA fragments (from different individuals) with altered mobility in the DGGE assay will reveal the precise sequence differences among them (see example 37, Variance Detection by DNA Sequencing). From the nucleic acid sequence data, the amino acid sequence can be determined and any amino acid differences can be identified.

The DGGE method is suitable for analysis of restriction enzyme digested genomic DNAs, as initially described by Lerman and co-workers (supra) and later extended (Gray, M. Detection of DNA Sequence Polymorphisms in Human Genomic DNA by Denaturing Gradient Blots, American Journal of Human Genetics, 50: 331-346, 1992). DGGE is equally suitable for analysis of cloned DNA fragments or DNA fragments produced by PCR. The analysis of cloned fragments or PCR fragments has the advantage that non-natural sequences, rich in G and C nucleotides can easily be added to the 5' ends (either flanking the cloning site or at the 5' ends of PCR primers). Such DNA fragments have very stable double stranded segments, called GC clamps, at one or both ends. The GC clamps alter the melting properties of the fragments, and can be designed so as to insure melting of the inter-primer segment of the PCR product at a lower temperature than the clamps, thereby optimizing the detection of sequence differences (see Myers et alia, supra and Myers et alia, Nearly All Single Base Substitutions in DNA Fragments Joined to a GC Clamp Can be Detected by Denaturing Gradient Gel Electrophoresis. Nucleic Acids Research 13: 3131, 1985). GC clamps can be rationally designed for any specific DNA fragment of known sequence by use of a computer program (MELT87, written by L. Lerman) that accurately predicts melting behavior based on analysis of primary sequence. When GC clamps are used correctly, the DGGE method is highly efficient at detecting DNA sequence differences. Not only are nearly 100% of differences detected, but the false positive rate is essentially zero. (Abrams, E.S., et alia, Comprehensive Detection of Single Base Changes in Human Genomic DNA Using Denaturing Gradient Gel

Electrophoresis and a GC Clamp. Genomics 7: 463-475, 1990.) Recently methods for increasing the throughput of DGGE have been developed, based on multiplex PCR.

The steps in carrying out DGGE with GC clamps are:

5

10

15

- 1. Design DNA fragments with optimal melting behavior. Select oligonucleotide primers, using GC clamps as necessary, to produce a single melting domain over the length of the sequence to be analyzed. (It may be necessary to divide the sequence into overlapping fragments to achieve this goal.) Design of primers and simulated analysis of fragments can be performed with the computer program described by Lerman. (Lerman, L.S. and Silverstein, K. Computational Simulation of DNA Melting and its Application to Denaturing Gradient Gel Electrophoresis. Methods in Enzymology 155: 482-501, 1987.) The output of the program is the melting map of the fragment, from which it will also be possible to determine the optimal range of denaturant in the gradient and the approximate electrophoresis time for fragments to reach the point of melting in the gradient.
- 2. Amplify the fragment by PCR. Procedures for optimizing PCR are briefly described in other examples and are well known in the art. Template DNA samples can either be cDNA or genomic DNA and will typically be drawn from a panel of unrelated individuals.

20

25

3. Pour a denaturing gradient gel. Briefly, make up two gel solutions containing the desired beginning and end concentrations of denaturant. The gel solutions are generally made up by mixing "0%" and "100%" denaturant stock solutions, where the 0% stock consists of 7% acrylamide in Tris-acetate EDTA (TAE) electrophoresis buffer, and the 100% stock is also 7% acrylamide in TAE, plus 40% formamide by volume and 7 molar urea. Equal volumes of the two solutions (e.g. twelve milliliters of each solution) are poured into the two chambers of a gradient maker (usually between 20 and 40% denaturant in the upstream chamber and 60 to 80% in the lower

232/116

one) immediately after addition of ammonium persulfate and TEMED for acrylamide polymerization. Open the stopcock of the gradient maker and pour the gradient gel. Usually gels are .75 to 1 mm in thickness, and gel combs that form 10-30 wells are used. With commercially available apparatus multiple gradient gels can be poured simultaneously. Suitable apparatus is sold by several vendors, including the BioRad (Hercules, CA) Dcode system and the C.B.S. Scientific DGGE system.

5

10

15

20

25

- 4. Place the gel in a heated bath of electrophoresis buffer. Gels are electrophoresed at elevated temperature which, together with the denaturant, brings the DNA fragments to their melting point. Gels are often run at 60°C in 1X TAE buffer, with constant recirculation of buffer to the upper buffer chamber. Once the gel has been placed in the heated tank and allowed to equilibrate it can be loaded. Multiple gels can be run simultaneously in the same tank with the apparatus listed above.
- 5. Load and run gel. Usually enough PCR product from each sample is loaded on the gel so that samples can be detected by a simple DNA staining procedure; use of radioactivity, dyes or hybridization procedures can thereby be avoided. At least 100 mg of each sample should be loaded, but preferably over 200 ng. Gel running conditions can be estimated from the output of the MELT87 program, however empirical adjustment will often be necessary. Usually a voltage of ~80 to 200V is applied for periods of 5-20 hours, depending on the characteristics of the fragments being analyzed.
 - 6. Stain and analyze gel. After electrophoresis gels are stained with ethidium bromide, SYBR Green, silver or some other procedure. The location of PCR products produced with the same primer pairs should be compared. Altered location, and usually the appearance of two or more bands instead of one, signify the presence of DNA sequence differences. (The reason for more than two bands from a diploid sample is that during the terminal cycle of heating and cooling of the PCR

10

15

20

25

step heteroduplexes are formed between the maternally and paternally inherited alleles. If those alleles differ in sequence, the heteroduplexes will have mispaired nucleotides at the sites of difference. As a result the heteroduplexes will be less stable than either of the homoduplex species, and will consequently melt and be retarded in the gel at a lower concentration of denaturant. Altogether one may see four bands in such samples: two reciprocol heteroduplexes and two homoduplexes.) The specific pattern of fragments in each lane constitutes a signature for a specific nucleotide change.

7. Sequence DNA fragments with altered mobility. Examples of all different signatures should next be analyzed by DNA sequencing to identify the base difference(s) accounting for altered mobility in the gradient gel. See example 37 for a description of this procedure and the subsequent steps of recording the sequence variances and analyzing their frequency and structural and functional consequences.

Example 37: Variance detection by sequencing.

Sequencing by the Sanger dideoxy method or the Maxim Gilbert chemical cleavage method is widely used to determine the nucleotide sequence of genes. Presently, a worldwide effort is being put forward to sequence the entire human genome. The Human Genome Project as it is called has already resulted in the identification and sequencing of many new human genes. Sequencing can not only be used to identify new genes, but can also be used to identify variations between individuals in the sequence of those genes.

The following are the major steps involved in identifying sequence variations in a candidate gene by sequencing:

WO 98/41648

295 232/116

- Amplification by the polymerase chain reaction (PCR) of 400-700 bp regions
 of the candidate gene from a panel of DNA samples. The DNA samples can
 either be cDNA or genomic DNA and will represent some cross section of
 the world population.
- 2. Sequencing of the resulting PCR fragments using the Sanger dideoxy method. Sequencing reactions are performed using flourescently labeled dideoxy terminators and electrophoresedon an ABI 377 sequencer or its equivalent.
- 3. Analysis of the resulting data from the ABI 377 sequencer using software programs designed to identify sequence variations between the different samples analyzed.

A more detailed description of the procedure is as follows:

A candidate gene sequence is downloaded from an appropriate database. Primers for PCR amplification are designed which will result in the target sequence being divided into amplification products of between 400 and 700 bp. There will be a minimum of a 50 bp of overlap not including the primer sequences between the 5' and 3' ends of adjacent fragments to ensure the detection of variances which are located close to one of the primers.

20

25

15

5

10

Optimal PCR conditions for each of the primer pairs is determined experimentally. Parameters including but not limited to annealing temperature, pH, MgCl₂ concentration, and KCl concentration will be varied until conditions for optimal PCR amplification are established. The PCR conditions derived for each primer pair is then used to amplify a panel of DNA samples (cDNA or genomic DNA) which is chosen to best represent the various ethnic backgrounds of the world population or some designated subset of that population.

PCR reactions are purified using the QIAquick 8 PCR purification kit (Qiagen cat#

WO 98/41648

296

232/116

28142) to remove nucleotides, proteins and buffers. The PCR reactions are mixed with 5 volumes of Buffer PB and applied to the wells of the QIAquick strips. The liquid is pulled through the strips by applying a vacuum. The wells are then washed two times with 1 ml of buffer PE and allowed to dry for 5 minutes under vacuum. The PCR products are eluted from the strips using 60 ul of elution buffer.

5

The purified PCR fragments are sequenced in both directions using the Perkin Elmer

ABI PrismTM Big DyeTM terminator Cycle Sequencing Ready Reaction Kit (Cat# 4303150). The following sequencing reaction is set up: 8.0 ul Terminator Ready Reaction Mix, 6.0 ul of purified PCR fragment, 20 picomoles of primer, deionized water to 20 ul. The reactions are run through the following cycles 25 times: 96°C for 10 second, annealing temperature for that particular PCR product for 5 seconds,

60°C for 4 minutes.

15

10

The above sequencing reactions are ethanol precipitated directly in the PCR plate, washed with 70% ethanol, and brought up in a volume of 6 ul of formamide dye. The reactions are heated to 90°C for 2 minutes and then quickly cooled to 4°C. 1 ul

of each sequencing reaction is then loaded and run on an ABI 377 sequencer.

20

25

The output for the ABI sequencer appears as a series of peaks where each of the different nucleotides, A, C, G, and T appear as a different color. The nucleotide at each position in the sequence is determined by the most prominent peak at each location. Comparison of each of the sequencing outputs for each sample can be examined using software programs to determine the presence of a variance in the sequence. One example of heterozygote detection using sequencing with dye labeled terminators is described in Pui-Yan Kwok et. al. (Pui-Yan Kwok, Christopher Carlson, Thomas D. Yager, Wendy Ankener, and Deborah A. Nickerson, Genomics 23, 138-144 (1994)). The software compares each of the normalized peaks between all the samples base by base and looks for a 40% decrease in peak height and the concomitant

297 232/116

appearance of a new peak underneath. Possible variances flagged by the software are further analyzed visually to confirm their validity

5

Example 38. Loss of heterozygosity.

10

15

20

25

Loss of chromosomes or segments of chromosomes in disease cells results in loss of alleles in the disease cells compared to normal diploid cells. Such allele losses are a common occurrence in cancer, where they have been documented in over 1,500 publications in the past 14 years. More recent work has documented the occurrence of allele loss in other proliferative diseases. Several cytogenetic and molecular techniques have been developed to measure chromosome losses. The molecular techniques are preferable for identification of allele loss because they also show which allele is lost, and are therefore best suited to provide the information needed to implement the present invention.

In order to measure chromosome loss using molecular techniques it is necessary to be able to distinguish the paternally and maternally inherited copies of a given chromosome. DNA variances allow the two copies of a given chromosome to be distinguished because different alleles can be resolved electrophoretically. The standard method for analyzing allele loss in cancer is to compare tumor cell DNA with normal cell DNA, either in a Southern blot or using PCR based techniques. A patient's tumor DNA is said to be "informative" for allele loss only at loci where the patient's normal cells are heterozygous. When such heterozygous loci are examined in tumor cells often only one allele is detected. Such tumor cells have lost the heterozygous state which characterizes all normal somatic cells of the patient, hence the term loss of heterozygosity (LOH).

PCT/US98/05419 WO 98/41648

298

232/116

Several effective molecular procedures have been developed to measure LOH. These procedures have been applied most extensively to cancer tissues, however the same methods are effective in the study of nonmalignant diseases such as atherosclerotic plaques and endometriosis. The main steps are:

5

1. Identify DNA variances at or near the locus to be investigated for LOH.

10

obtained by measuring the frequency of LOH at neighboring polymorphic markers on the same chromosome, or more preferably on the same chromosome arm, or most

LOH usually affects large segments of DNA, ranging from several megabases to an entire chromosome. As a result, accurate estimation of LOH at a specific locus can be

preferably within several 10-20 megabases of the locus. However, to precisely

measure LOH at a specific locus requires a variance at the locus. Different types of

15

variances have been used to study LOH, including single nucleotide polymophisms (SNPs), specifically SNPs that alter restriction endonuclease cleavage sites, called

RFLPs. (For details of this approach see Vogelstein, B., et al., Allelotype of colorectal

carcinomas. Science 244: 207-211, 1989). Also short tandem repeat polymorphisms

(STRPs), including di-, tri- and tetranucleotide repeat polymorphisms have been used

to measure LOH. (For details of this procedure see Jones and Nakamura, Deletion

20

Mapping of Chromosome 3p in Female Genital Tract Malignancies Using

Microsatellite Polymorphisms. Oncogene 7: 1631-1634, 1992.) Procedures for

identifying variances are described in Examples 28, 29, 30 and 36.

25

2. Prepare DNA from paired normal and disease tissue samples from patients being studied.

Before preparing genomic DNA from tumor tissue it is important to assess tumor cell purity and viability, using microscopic examination of frozen sections if necessary. If embedded pathological specimens are being analyzed tumor cell purity can be

299 232/116

assessed by examining histologic sections before selecting areas for cell isolation and DNA purification. (See Johnson, et al., Direct Molecular Analysis of Archival Tumor Tissue for Loss of Heterozygosity, BioTechniques 19:190-191, 1995, and references therein for description of techniques for purifying tumor cell DNA from archival pathology samples.) Areas of necrosis and extensive admixture of normal and tumor tissue should be avoided. For Southern blotting ~5-10 ug of genomic DNA is required for each sample being analyzed. For PCR based methods as little as 5 to 10 ng of genomic DNA is sufficient; much less will suffice if two successive rounds of PCR amplification are used.

5

10

15

20

25

3. Determine genotype in the normal and disease tissues using a quantitative or semiquantitative procedure that allows the amount of each allele to be measured. Compare the ratio of alleles in the normal tissue to the ratio in the tumor tissue

In order to show LOH at a given locus it is necessary to establish that the patient is constitutionally heterozygous at the locus. Thus DNA from normal tissue must be tested, either before or in parallel with tumor tissue DNA. A variety of methods can be used for quantitation of signal from the two alleles. If the alleles are compared on a Southern blot then signal in the bands corresponding to the two alleles can be counted by radioactive or nonradioactive techniques (see Ausubel, et al., Current Protocols in Molecular Biology, John Wiley & Sons). One method employs phosphor technology using a Molecular Dynamics PhosphorImager with ImageQuant software to measure signals. If the alleles are compared after PCR amplification then DNA sequencing can provide accurate quantitation of allele ratios. See, for example, Goldsborough and Komberg, Allele-Specific Quantification of Drosophila Engrailed and Invected Transcripts, Proc. Natl. Acad. Sci. U.S.A. 91:12696-12700, 1994.

Using highly variable markers distributed across the genome a comprehensive map of LOH can be assembled for a specific cancer type. Such data sets have been termed allelotypes. Separate studies are necessary for different cancer (or other disease) types

300 232/116

as the patterns of LOH differ significantly in different diseases.

Other techniques that have been used to detect allele loss in cancer include Comparative Genomic Hybridization (CGH) and Representation Difference Analysis (RDA) however these methods are more complex than the Southern blot or PCR based techniques. Chromosome loss can also be detected cytogenetically. Mitelman (Catalog of Chromosome Aberrations in Cancer. Wiley-Liss, New York, 1995.) has compiled a catalog of over 10,000 published karyotypes of cancer cells which documents chromosome deletions as well as other changes.

10

5

Example 39. Small molecule inhibitors of variant sequences:

Methylguanine Methyltransferase (MGMT)

Gene VARIA 1534

15

The methylguanine methyltransferase gene is essential for cell growth or survival in the presence of alkylating agents

20

25

Methylguanine methyltransferase (MGMT) is a nuclear protein that repairs alkylating agent damage, specifically alkylation of the O6 position of guanine bases in genomic DNA. MGMT acts as a suicide protein in removing methyl or alkyl groups from guanine and covalently binding them to cysteine 145 of MGMT. The protein is subsequently degraded; it does not act as an enzyme. O6-benzylguanine is an inhibitor of MGMT that mimics the natural substrate, alkylated DNA; transfer of the benzyl group to cysteine 145 of MGMT inactivates the protein. Concurrent administration of O6-benzylguanine and an alkylating agent such as carmustine (BCNU) or lomustine (CCNU) renders tumor cells more sensitive to the toxic effects of the nitrosoureas by inactivating MGMT and thereby inhibiting the tumor cells ability to repair alkylated

301 232/116

PCT/US98/05419

DNA. MGMT is thus a conditionally essential gene in the presence of nitrosoureas and other alkylating agents. The conditional essentiality of MGMT has been demonstrated in mice. Animals homozygous for disrupted MGMT genes are more than ten times as sensitive to alkylating agents as normal mice. The relative sensitivity has been measured as the LD50, the dose required to kill 50% of treated animals. (Tsuzuki, T., et al. Targeted disruption of the DNA repair methyltransferase gene renders mice hypersensitive to alkylating agent. *Carcinogenesis* 17: 1215-1220, 1996.) O6-benzylguanine is being developed as a chemosensitizing agent (with alkylating agents) for treatment of human cancer. This treatment regimen is not specific for cancer cells.

10

15

5

WO 98/41648

In a cancer patient with two alternative functional MGMT alleles in normal tissues and LOH at 10q23 resulting in only one copy of MGMT in cancer cells, an allele specific inhibitor of MGMT could be used to specifically sensitize cancer cells to the action of alkylating agents. Treatment would consist of the administration of the appropriate allele specific inhibitor (directed to the one allele remaining in cancer cells) plus an alkylating agent. The tumor cells would be unable to effectively repair the alkylating agent induced DNA damage, while the uninhibited allele in normal cells would be able to function. Thus normal cells, including sensitive normal cell populations such as bone marrow stem cells, would be able to tolerate higher doses of alkylating agents than cancer cells.

20

The MGMT gene and encoded protein are polymorphic

25

Four variances in human MGMT have been discovered by the inventors or reported in the literature, including three variances that affect the protein sequence. There is a C/T variance at nucleotide 255 (11% heterozygotes among 36 individuals surveyed) which does not affect the encoded protein. There is a second C/T variance at nt. 346 which results in a L84F amino acid variance (5% heterozygotes among 36 individuals surveyed). There is an A/G variance at nt. 523 which results in a I143V amino acid

variance (24% heterozygotes among 36 individuals surveyed). This variance occurs only two residues from the active site cysteine at 145. A fourth variance, G/A has been reported in the Japanese population at codon 160, GGA vs. AGA, resulting in a glycine vs. arginine amino acid variance. Fifteen percent of 40 Japanese individuals studied were heterozygotes for this variance. (Imai, Y., et al. A polymorphism at codon 160 of human O6-methylguanine-DNA methyltransferase gene in young patients with adult type cancers and functional assay. *Carcinogenesis* [London] 16:2441-24445, 1995.)

Allele specific inhibitors of MGMT

10

15

5

Two of the amino acid variances in MGMT, at residues 143 and 160, are near the active site of the protein. Substantial work has already been done to characterize the functional consequences of the residue 160 glycine/arginine variance. Studies of MGMT kinetics and activity have shown that the 160arginine allele is at least 20 fold more resistant to O6 benzylguanine inactivation, measured as an increase in the ED50 and or as a reduction in the production of guanine from O6-benzyl[8-3H] guanine. The 160gly and 160arg forms of MGMT were nearly equal in alkyltransferase activity in an assay that measured repair of O6-methylguanine in methylated DNA. These results demonstrate variance-specific effects of a small molecule, O6-benzylguanine, on normal (non-mutant) alleles of the conditionally essential MGMT gene. (Edara, S., et al. Resistance of the human O6-alkylguanine-DNA alkyltransferase containing arginine at codon 160 to inactivation by O6-benzylguanine. Cancer Research 56: 5571-5575, 1996)

25

20

Administration of O6-benzylguanine to patients who are heterozygous for the variance in their normal cells, and contain only the alternative form of the gene with a glycine residue at position 160 in their cancer cells, together with methylating or chloroethylating agents, will specifically sensitize cancer cells to the cytotoxic effects of the alkylating agents without increasing toxicity to normal cells which, since they

WO 98/41648

5

10

15

20

25

303 232/116

PCT/US98/05419

contain the O6-benzylguanine resistant 160arginine form of the protein, will continue to repair alkylated DNA.

There is no published data concerning the residue 143 variance, however the proximity of this variance to the active site - both in the primary sequence and upon inspection of the three dimensional structure of the bacterial AGT protein, a functional and structural homolog of human MGMT - suggests that allele specific drugs could be discovered for this variance.

The structural difference between 143isoleucine and 143valine is a hydrophobic methyl group. It is well known that most small molecule protein inhibitors interact via hydrophobic interactions. Favorable Van der Waals distances between hydrophobic groups of a substrate and a ligand are vital for high affinity interaction. One possible mechanism of allele specific inhibition would be to exploit the greater bulk of the isoleucine by finding a small molecule that fits into the active site pocket of the valine allele but has a very unfavorable Van der Waals interaction the methyl group of the isoleucine. Other schemes based on the different size and geometry of isoleucine and valine could also be effective.

One approach to identification of such inhibitors would be to make small molecule libraries in which various positions of guanine are substituted with moities of appropriate size and structure. Such libraries could then be tested in various screens of MGMT activity. The two alleles (143isoleucine and 143valine, or any of the other allele pairs of MGMT described above) would be assayed in parallel. Identification of molecules with allele specific inhibitory activity could be the basis for synthesis of additional libraries in which the moities that are best correlated with differential activity are further varied. Methods for the iterative design of high affinity or highly discriminating small molecule inhibitors are known in the art.

WO 98/41648

5

10

15

20

25

30

304 232/116

PCT/US98/05419

Libraries of restricted size can be screened for allele specific inhibitors using a combinatorial strategy based on known inhibitors of MGMT such as O6-benzylguanine. A library or libraries can be constructed in which substitutions are indroduced at positions C6 and N9 which have previouly been found to affect inactivation of MGMT, or at positions C2 and N8 which can be easily substituted. For example a series of 4(6)-(benzyloxy)-2,6(4)-diamino-5-(nitro or nitroso)pyrimidine derivatives and analogs in which 4(6)-benzyloxy groups were replaced with (2-, 3-, or 4 fluorobenzyl)oxy or (2-, 3-, or 4-pyridylmethyl)oxy groups have been synthesized and tested for MGMT inhibition. (Terashima I., and K. Kohda. Inhibition of human O6-alkylguanine-DNA alkyltransferase and potentiation of the cytotoxicity of chloroethylnitrosourea by 4(6)-(Benzyloxy)-2,6(4)-diamino-5-(nitro or nitroso)pyrimidine derivatives and analogues. *J Med Chem* 41: 503-508, 1998.) Substitutions at N7 have been found to be detrimental in general (Moschel, R.C. et al & Pegg, A. E., *J. Med. Chem.* 35: 4486-4491, 1992).

Combinatorial libraries can be constructed according to a published procedure (Norman, T. C. et al., A Structure-Based Library Approach to Kinase Inhibitors. *J. Am. Chem.Soc.* 118: 7430-7431, 1996) where guanine based libraries were made by anchoring a chemically modified guanine (at C6, C2, or C8) to solid supports at C2 via a glycinamide linkage or at N9 via a hydroxyethyl linkage. Chemical reactions can be carried out to introduce a library of hydrophobic substituents of different size at positions C6, C2, or C8. Hydrophobic substituents of various bulkiness and orientation can be indroduced through derivatives of O6-benzyl and O6-phenyl groups, O6-alkyl groups, N9-alkyl groups, and C2-amino-alkyl groups.

Libraries constructed as above can be screened for MGMT activity in several types of assays. Methods for bacterial expression and purification of human MGMT protein have been described (see Edara, et al., cited above). Both allelic forms of MGMT could be screened for repair of alkylated or methylated DNA by measuring transfer of tritium from a tritium labelled (methylated) DNA substrate in the

305 232/116

presence of various concentrations of library compounds for various times.

Alternatively, library compounds could be tritiated and MGMT proteins could be screened for the rate at which they interact with (either via association or cleavage of a moiety from the compound). Other assays for MGMT activity are known in the art.

Example 41. Clinical use of variance specific inhibitors for treating cancer

Inhibitors that are the object of the present invention are designed to be administered to patients who are heterozygous for the target gene, meaning that their cells normally contain two alternative copies of the gene, one that is sensitive to inhibition by said inhibitors, and one that is not sensitive to said inhibitors. It is apparent that several such inhibitors may be developed according to this invention targeted to alternative alleles of a single target gene or to several different target genes. The inventors propose that a series of such inhibitors will be developed according to this invention.

The clinical use of this invention involves the steps of:

5

10

15

20

25

- (a) testing normal cells from a patient to identify target genes that are heterozygous, present in two alternative forms.
- (b) testing biopsy tissue from a tumor or proliferative lesion to determine whether one of the two alternative forms is eliminated due to LOH.
- (c) selecting a drug for inhibition based on the presence of the sensitive allele in the tumor and the presence of an insensitive allele in normal cells
- (d) administering said drug to the patient in an appropriate dose to inhibit the essential function in the cancer cell.

Testing of normal cells to identify heterozygosity of the target gene is performed

306 232/116

PCT/US98/05419

using conventional diagnostic methods that are known in the art. Normal cells are commonly derived from a blood sample, hair sample, or buccal smear.

Alternatively normal cells may be obtained by cultivating primary cells such as lymphoblasts or fibroblasts in vitro. The presence of two alternative alleles may be determined by methods including allele-specific hybridization with oligonucleotides containing the variant sequences and a number of non-variant nucleotides to allow differential binding to the alternative forms of the gene or other methods known in the art using purified DNA or RNA or amplified DNA or cDNA sequences. Testing of biopsy tissue is performed by separating tumor cells or cells of the proliferative lesion to isolate a sample of cells characteristic of the proliferative lesion for analysis. This is performed by a variety of methods known in the art including manual dissection or laser assisted methods for eliminating normal cells or selecting abnormal cells. Samples of abnormal tissue, and samples of normal tissue as a control, are analyzed to identify the presence or absence of alternative forms of the target gene. The presence of two altrnative alleles may be determined by methods including allele-specific hybridization with oligonucleotides containing the variant sequences and a number of non-variant nucleotides to allow differential binding to the alternative forms of the gene or other methods known in the art using purified DNA or RNA or amplified DNA or cDNA sequences.

20

25

5

10

15

WO 98/41648

Selection of a drug for administration will be based on clinical trial data indicating that the drug is effective in eliminating abnormally proliferating cells and causing an improvement in the patient's clinical condition for patients who have the sensitive allele of the target gene in their pathological lesion. In one aspect of this invention, the product label will describe that the drug is indicated in patients who have only a specific allele of the target gene in their lesion and an alternative allele in their normal cells. Any such drug will be indicated only for a fraction of patients having two alternative alleles of the target gene in their normal cells and LOH. The fraction of patients who may be treated with any one drug may be determined by

PCT/US98/05419

232/116

multiplying the number of patients with a given cancer times the fraction of tumors exhibiting LOH of the target gene locus times the fraction of patients who will be heterozygous. For a target gene exhibiting 50% heterozygosity in the population and a 70% fraction of LOH in a specific cancer (several such examples are shown), a single inhibitor will treat ~17% of such cancers. A second compound directed against the alternative allele would treat another 17% of said cancer. In the preferred use of this invention, a panel of such drugs will be available enabling therapy with at least one such drug in most patients.

Administration of the drug to the patient ration to the patient will involve conventional means such as parenteral, oral, or intratumoral administration. The route of administration will be determined separately for each inhibitor and will be based on the bioavailability of the compound to the lesion. The compound may be administered in one or more doses as a single agent or in combination with other allele specific agents or conventional antiproliferative drugs or agents commonly used for the treatment of cancer or support of cancer patients.

Example 42. Cell Division Cycle 25C (CDC25C) - Gene VARIA10

Cdc25C is essential for cell growth

WO 98/41648

5

10

15

20

25

A vital regulator of cell proliferation is the protein kinase Cdc2, whose activation at the end of G2 of the cell cycle initiates mitosis. Gene disruption experiments in yeast confirm the importance of this protein, as cells lacking Cdc2 fail to progress through the cell cycle. As would be expected for such an important protein, Cdc2 activity is tightly regulated. Its activity depends on complex formation with Cyclin B, a protein that accumulates through the cell cycle and is then abruptly degraded during mitosis. Phosphorylation of Cdc2 on Tyr-15 and Thr-14 by the Wee1/Mik1

PCT/US98/05419

232/116

kinases maintains the Cdc2/Cyclin B complex in an inactive state until the end of G2. The dual-specificity phosphatase Cdc25C is then stimulated to dephosphorylate Cdc2 on both residues, resulting in activation of the complex. Just as Cdc2 is essential for cell growth, the regulation of its activity is essential. The best evidence for this is that the individual disruption of cdc2, cyclin B, wee 1 and cdc25 in the yeast *S. pombe* are lethal events. When cdc25 is deleted from these cells they display a phenotype consistent with their function; they grow without dividing, becoming dramatically elongated.

The human CDC25C gene and protein have variances

WO 98/41648

5

10

15

20

25

The CDC25C cDNA was cloned by Sadhu et al. (1) (Genbank accession number M34065, GI number 181075). To determine whether CDC25 is polymorphic, VARIAGENICS scanned cDNA from 32 unrelated individuals using the T4 Endonuclease VII method, which involves the cleavage of DNA heteroduplexes followed by DNA sequencing of polymorphic regions (see description of method in examples). A transversion at nucleotide 1099 (G or C) was identified (nucleotide numbering is from reference 1). This results in an amino acid difference at residue 297, with G encoding glycine and C encoding arginine. Overall, 9.4% of individuals analyzed are heterozygous. The rate of heterozygosity increases to 33.3% in Caucasians.

The human CDC25C gene maps to chromosome 5q31, a site of frequent loss of heterozygosity

Sartor *et al.* (2) mapped the human CDC25 gene to 5q31 by fluorescence in situ hybridization using the cDNA cloned by Sadhu *et al.* This mapping location was confirmed by Taviaux and Demaille (3), also using fluorescence in situ hybridization. There have been many studies of LOH on 5q, particularly the 5q21-

q22 region where the Adenomatous Polyposis Coli (APC) tumor suppressor gene lies. The most extensively studied cancers are those of the gastrointestinal tract, lung and ovary. There have been fewer studies of the 5q23-q33 region just distal to APC (where CDC25C lies), however the available data suggests that LOH occurs in this region at a frequency of ~30% in cervical cancer (4), 20-40% in colon cancer (5,6), 30-50% in ovarian cancer (7,8), up to 38% in stomach cancer (9), and 23% in testicular cancer (10). There is also evidence for LOH in head and neck, lung and liver cancers. In most of these studies only one or two markers were used. Definitive assessment of LOH frequency at the CDC25C locus will require direct analysis of the polymorphisms identified in various tumor types.

References

5

10

15

20

- 1) Sadhu, K., Reed, S.I., Richardson, H., Russell, P. (1990) Human homolog of fission yeast cdc25 mitotic inducer is predominantly expressed in G(2). *Proc. Natl. Acad. Sci. U.S.A.* 87: 5139-5143.
- 2) Sartor, H., Ehlert, F., Grzeschik, K.-H., Muller, R., Adolph, S. (1992) Assignment of two human cell cycle genes, CDC25C and CCNB1, to 5q31 and 5q12, respectively. *Genomics* 13: 911-912.
- 3) Taviaux, S.A., Demaille, J.G. (1993) Localization of human cell cycle regulatory genes CDC25C to 5q31 and WEE1 to 11p15.3-11p15.1 by fluorescence in situ hybridization. *Genomics* 15: 194-196.
- 4) Mitra, A.B., Murty, V.V., Li, R.G., Pratap, M., Luthra, U.K., Chaganti, R.S. (1994) Allelotype analysis of cervical carcinoma. *Cancer Res.* 54: 4481-7.
- 5) Japanese Journal of Cancer Research 82:1003.
- 6) Cunningham, C., Dunlop, M.G., Wyllie, A.H., Bird, C.C. (1993) Deletion mapping in colorectal cancer of a putative tumour suppressor gene in 8p22-p21.3.

 Oncogene 8: 1391-6.
 - 7) British Journal of Cancer 69: 429.
 - 8) Weitzel, J.N., Patel, J., Smith, D.M., Goodman, A., Safaii, H., Ball, H.G. (1994)

310 232/116

Molecular genetic changes associated with ovarian cancer. *Gynecol. Oncol.* 55: 245-52.

9) Genes, Chromosomes and Cancer 3: 468.

10) Murty, V.V., Bosl, G.J., Houldsworth, J., et al. (1994) Allelic loss and somatic differentiation in human male germ cell tumors. *Oncogene* 9: 2245-51.

Example 43. Dihydropyrimidine Dehydrogenase (DPD)

DPD is conditionally essential

Dihydropyrimidine Dehydrogenase is essential for cell survival in the presence of pyrimidine nucleotide analogs such as 5-FU and fluorodeoxyuridine. 5-fluorouracil (5-FU) and related compounds are antineoplastic drugs used in the treatment of breast, gastrointestinal, head and neck and other cancers. These drugs have widely varying clinical effects in cancer patients, ranging from induction of complete response (tumor disappearance) in some patients to severe toxicity in others. There is currently no reliable basis for predicting individual patient responses, and therefore patients receiving 5-FU must be monitored carefully for toxic reactions.

20

25

5

10

15

There are a variety of anabolic and catabolic pathways that affect the action of 5-FU (reviewed in Goodman and Gilman, The Pharmacological Basis of Therapeutics, 8th edition). For example, in order to exert its antiproliferative effects the pyrimidine analog 5-FU must be converted enzymatically to the nucleotide level (fluorodeoxyuridine) by phosphorylation and ribosylation; fluorodeoxyuridine is sometimes given directly because it bypasses most of these steps, and simply requires phosphorylation by thymidine kinase. The 5-fluoronucleotide is an irreversible inhibitor of thymidylate synthase, the enzyme which converts dUMP to dTMP and is required for de novo synthesis of thymidine, and hence for DNA

311 232/116

synthesis.

5

10

15

20

There is a three step pathway for catabolism of pyrimidines (thymine and uracil) to beta alanine. Pyrimidine analogs such as 5-FU are catabolized by the same pathway. The first and rate limiting step in this pathway is catalyzed by dihydropyrimidine dehyrogenase (DPD). DPD accounts for catabolism of as much as 90% of a 5-FU dose in normal individuals, and the half life of 5-FU in normals is ~8-20 minutes. Patients homozygous for mutant DPD alleles have been identified, a condition variously called DPD Deficiency, Hereditary Thymine-Uraciluria or Familial Pyrimidinemia. In such patients ~90% of 5-FU is excreted unchanged in the urine, and the drug has a half life longer that 2.5 hours. As a result of the drastically reduced catabolism of 5-FU the toxic effects of the drug are magnified and patients are subject to severe toxic reactions. There are reports of deaths in patients with DPD deficiency after treatment with 5-FU. Thus cell (and organism) survival in the presence of 5-FU depends on presence of functional DPD protein to transform 5-FU to the inactive dihydroxy metabolite.

This principal has also been demonstrated in cancer cells both in vitro and in vivo: cancer cells with lower DPD levels are more susceptible to the toxic effects of 5-FU. It has been suggested that measuring DPD levels would be useful for calibration of 5-FU dosage.

The DPD gene exhibits variances

We have identified four common sites of variance in DPD mRNA by screening cDNA from 36 unrelated individuals. The variant nucleotides are 166, 577, 3925 and 3937 (see DPD Variance Table; numbering is from Yokota, et al. cDNA Cloning and Chromosome Mapping of Human Dlhydropyrimidine Dehydrogenase, an Enzyme Associated with 5-fluorouracil Toxicity and Congenital Thymine

10

15

20

25

Uraciluria. Journal of Biological Chemistry. 269: 23192-23196, 1994). Two of the variances in nucleotide sequence alter the amino acid coding sequence: amino acid 29 is usually cysteine but arginine alleles were also detected; cys/arg heterozygotes were found at a frequency of 11%. Residue 166 of DPD is reported to be methionine but valine is present at 166 in some alleles; 9% of the population surveyed are met/val heterozygotes. One double heterozygote was identified out of 36 patients. Both these amino acid polymorphisms are located in the N-terminal NAD/FAD binding domain of DPD. Residue 166 is located in a highly conserved domain of DPD. Two other polymorphisms are located in the 3' untranslated region of DPD, only 11 nucleotides apart.

The DPD gene maps to chromosome 1p22, a region frequently subject to LOH in different cancers

The DPD gene has been mapped to chromosome 1p22 by fluorescense in situ hybridization. LOH at 1p22 has been reported in colon, breast, and other cancers.

Allele specific inhibition of DPD to potentiate 5-FU action in cancer cells with LOH at the DPD locus

The DPD gene is polymorphic and conditionally essential in the presence of 5-FU. These properties can be exploited in a therapeutic strategy for cancer patients with LOH at the DPD locus. Specifically, in a patient with two alternative alleles for DPD in normal cells and one allele in cancer cells due to LOH, an allele specific drug can be used to sensitize cancer cells to the action of 5-FU by inhibiting its catabolism. Cancer cells (but not normal cells) would be poisoned by high levels of 5-FU due to low clearance. Normal cells, containing an uninhibited allele, would be able to catabolize DPD at close to normal levels.

Alternatively, patients heterozygous for functional and defective copies of DPD,

232/116

PCT/US98/05419

and in whom LOH resulted in loss of the functional allele, could be treated by 5-FU without the necessity for an allele specific inhibitor. Identification of such patients would require a test for heterozygosity at DPD and a test for LOH which could show which allele is deleted in cancer cells. Such an approach would be expected to identify patients likely to respond well to 5-FU even though they might have cancers not traditionally treated with pyrimidine analogs.

Example 44. Fanconi Anemia genes A, B, C, D, E, F, G and H (FAA, FAB, FAC, FAD, FAE, FAF, FAG, FAH)

The Fanconi Anemia genes are conditionally essential.

WO 98/41648

5

10

15

20

25

The Fanconi Anemia genes are essential for cell growth or survival in the presence of DNA cross linking agents. In order for cells to survive or proliferate in an abnormal environment characterized by the presence of DNA cross linking molecules such as Mitomycin C and diepoxybutane it is necessary that the cells are capable of efficiently repairing damage caused by these agents. Cells contain proteins necessary for such repair. One way such repair proteins can be identified is by absence of function in specific patients who, as a consequence, are particularly susceptible to the toxic effects of cross linking agents.

Fanconi Anemia (FA) is a hereditary disease, autosomal recessive in transmission, characterized by progressive bone marrow failure, birth defects and predisposition to malignancies. FA patients are hypersensitive to the toxicity of DNA cross linking agents. This hypersensitivity can be measured in cultured FA cells, which is one method used to establish the diagnosis of FA.

Patients heterozygous for defective FA genes are generally not hypersensitive to

232/116

DNA crosslinking agents in contrast to those that are homozygous. This suggests that treating heterozygous cancer patients with an inhibitor specific for one allele of the FA gene (and thereby reducing levels of FA protein function by up to 50% in normal cells) would be well tolerated. Inhibition of the FA allele present in cancer cells but not the alternative form present only in normal cells would make cancer cells selectively sensitive to crosslinking agents, leading to a cytotoxic antiproliferative effect. Normal cells would be able to repair damage caused by such agents, by analogy to the clinical data from patients heterozygous for defective FA genes.

10

15

5

The FA genes and gene products are polymorphic

Seven FA genes have been identified by complementation studies. The genes for FAA and FAC have been cloned. DNA variances have been reported in both genes. For example, Savino et al. report three variances in FAA, all of which alter the protein coding sequence. (Savino, M., et al. Mutations in the Fanconi Anemia Group A Gene (FAA) in Italian Patients. American Journal of Human Genetics 61:1246-1253, 1997.) The location of these variances is shown in the Table below, reproduced from the paper by Savino.

20

Variances in the FAA Gene

Polymorphic	Alternate	Affected amino	Alternate	Frequency of
nucleotide	bases	acid residue	amino acids	rare allele
796	A, G	266	Thr, Ala	.29
1501	G, A	501	Gly, Ser	.40
2426	G, A	809	Gly, Asp	.30

25

FA genes map to chromosomes that are frequently subject to LOH in different cancers

30

The FAC gene maps to chromosome 9q22.3, (as do three other FA complementation

315

232/116

groups according to Strathdee, C.A., et al. Evidence for at least four Fanconi anaemia genes including FACC on chromosome 9. Nature Genetics 1: 196-198, 1992). The FAA gene maps to chromosome 16q24.3. FAD maps to 3p26-p22. All FA genes mapped so far lie in regions subject to frequent LOH. LOH affecting chromosome 9 is well documented in many cancers. For example, loss of the 9q arm is well documented in cancers such as bladder, esophagus, ovary, testis and uterus. LOH frequencies in these cancers range from 20% to 62%. LOH affecting chromosome arm 16q, particularly the 16q24 region is well documented, particularly in breast, prostate and liver cancers. For example, in six detailed studies of breast cancer in the 16q22-q24 region LOH frequencies of 40-60% have been reported. Further, 16q22 LOH has been reported in 25-90% of liver cancers, with the average around 45%. Less extensive studies of other cancer types report 16q22 LOH in 19% of bladder cancers, 20% of colon cancers, 19-27% of esophageal cancers, 25% of small cell lung cancers, 16-37% of ovarian cancers 22% of uterine cancers, and 31-50% of prostate cancers. Loss of chromosome 3p26-21 is common in lung cancer, kidney cancer, head and neck cancer and breast cancer among other cancers. Reports of >50% LOH are common in these cancer types.

Other genes conditionally essential for response to DNA cross linking agents

20

25

5

10

15

In a related aspect, other genes which, when defective, sensitize cells to toxic effects of DNA crosslinking agents would be amenable to the therapeutic strategy outlined above for the FA genes. Specifically, in a patient with two alternative alleles for such a gene and LOH at the relevant locus, an allele specific drug could be used to sensitize cancer cells to the action of cross linking agents. Such drugs could then be used to treat cancer patients constitutionally heterozygous for two normal alleles at the relevant locus, in whom LOH had rendered cancer cells hemizygous or homozygous for one allele. Treatment would consist in the administration of the appropriate allele specific inhibitor plus a cross linking agent or treatment to induce damage in all cells. Cancer

316

232/116

cells (but not normal cells) would be rendered unable to respond by inhibition of expression of the relevant repair gene. Examples of such genes are the excision repair cross complementing (ERCC) genes, twelve of which have been identified (see Target Gene Table). Defects in these genes are associated with Xeroderma Pigmentosum and Cockayne Syndrome. (Scriver, C. R. et al., The Metabolic and Molecular Bases of Inherited Disease, 7th edition, McGraw Hill, New York, 1995.)

Alternatively, patients heterozygous for functional and defective copies of such genes, and in whom LOH resulted in loss of the functional allele, could be treated by a cross-link inducing procedure without the necessity for an allele specific inhibitor. Identification of such patients would require a test for heterozygosity at the target locus and a test for LOH which could show which allele is deleted in cancer cells. Such an approach would be expected to identify patients likely to respond well to cross linking agents or procedures even though they might have cancers not traditionally treated with such agents.

Example 45. Asparagine Synthetase (AS). Variagenics Target Gene _____

5

10

15

20

25

Asparagine Synthase is conditionally essential

Cells require a continuous supply of amino acids for protein biosynthesis. Cells can import amino acids from serum via amino acid transporters (the only source besides protein catabolism for the ten essential amino acids), or amino acids cells can be synthesized *de novo* by cells (only an option for the ten nonessential amino acids). The essential amino acids are isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine and histidine. Alterations in the nutritional environment of growing cells that result in a decreased extracellular concentration of essential amino

317

232/116

acids cause arrested cell growth and may result in cell death.

5

10

15

20

25

Even a nonessential amino acid can become essential in a cell where (i) at least one enzyme required for its biosynthesis is not expressed (perhaps due to downregulation in response to an abundant extracellular supply of the amino acid), or (ii) the biosythetic pathway is blocked by an inhibitor.

Asparagine is a nonessential amino acid which is, however, essential for survival of rapidly dividing cells that are not expressing asparagine synthetase, the terminal enzyme in asparagine biosynthesis. Asparagine synthetase, considered to be a housekeeping gene, catalyzes the ATP dependent conversion of aspartic acid to asparagine in mammalian cells. A number of different cancer types do not usually express asparagine synthetase, including childhood acute leukemias. One common therapeutic used in the treatment of childhood acute lymphocytic leukemia is the enzyme L-asparaginase (purified from E. coli or Erwinia carotovora) which, upon injection, rapidly depletes serum asparagine (by hydrolysis to aspartate), thereby lowering blood levels of asparagine to undetectable levels within hours of injection. (Ohnuma, T. et al. Biochemical and Pharmacological Studies with L-Asparaginase in Man. Cancer Research 30: 2297-2305, 1970.) Leukemic cells have high rates of protein synthesis but do not express asparagine synthesase and are therefore highly vulnerable to the rapid loss of asparagine and consequent shutdown of protein synthesis. Cell death after L-asparaginase induced asparagine starvation has been shown to be apoptotic. (Bussolati, O. Characterization of Apoptotic Phenomena Induced by Treatment with L-Asparaginase in NIH3T3 Cells. Experimental Cell Research 220: 283-291, 1995.) After one or more doses leukemic cells often become resistant to L-asparaginase due to induction of asparagine synthetase activity and consequent autonomy for asparagine.

In a patient with two alternative alleles for asparagine synthetase and LOH at 7q, an

10

15

20

25

allele specific drug could be used to sensitize cancer cells to the action of L-asparaginase. Such drugs could then be used to treat cancer patients constitutionally heterozygous for two normal alleles at the asparagine synthetase locus, in whom LOH had rendered cancer cells hemizygous or homozygous for one allele. Treatment would consist in the administration of the appropriate allele specific inhibitor plus L-asparaginase to deplete the concentration of this amino acid in serum while rendering cancer cells (but not normal cells) unable to respond by upregulating asparagine synthetase.

The Asparagine Synthetase gene maps to chromosome 7q21.3, a region frequently subject to LOH in different cancers

The asparagine synthetase gene has been mapped to chromosome 7q21.3 by fluorescence in situ hybridization, following localization to 7q by analysis of somatic cell hybrids. The q21 region of chromosome 7 is subject to frequent LOH, particularly in colon, breast and prostate cancers. 7q21.3 LOH is detected in up to 50% of colon cancers, up to 37% of prostate cancers (83% of prostate cancers have LOH in the adjacent chromosome band, 7q31) and in 10-55% of breast cancers, where again, there is even more frequent LOH in 7q31. LOH at 7q21 has also been reported in uterine cancer and head and neck cancer. Several other cancer types have not yet been well studied for LOH affecting this region.

Example 46. Methionine Synthase (MS).

Variagenics Target Gene _____

Methionine Synthase is conditionally essential in dividing cells

Cells require a continuous supply of amino acids for protein biosynthesis. L-

methionine is one of ten essential amino acids. Consequently dividing cells must obtain their methionine from serum via amino acid transporter (the only source besides protein catabolism for the ten essential amino acids). Alterations in the nutritional environment of growing cells that result in a decreased extracellular concentration of essential amino acids such as methionine cause arrested cell growth and may result in cell death. Cancer cells are particularly sensitive to methionine deprivation. (Tan, Y., et al., Anticancer Efficacy of Methioninase in vivo. *Anticancer Research* 16: 3931-3936.)

5

10

15

20

25

The cellular requirement for methionine can be bypassed: if L-homocysteine is provided to cells it can be methylated to form methionine by the enzyme methionine synthase (MS). In this reaction the methyl group is provided by 5-methyltetrahydrofolate and MS-bound methylcobalamin serves as an intermediate methyl carrier. A second enzyme may be required for reductive activation of methionine synthase, based on complementation studies.

It occured to the inventors that the apparent antineoplastic effects of methionine deprivation could be enhanced and made tumor cell specific by preventing cells from converting endogenous homocysteine to methionine by allele specific inhibition of methionine synthase (or other enzymes required for the conversion of homocysteine to methionine; see: Scriver, C., et al., editors, The Metabolic and Molecular Basis of Inherited Disease. McGraw Hill, New York, pp. 3111-3128 and 3129-3149). This strategy would be useful in cancer patients that are heterozygous for methionine synthase (or another enzyme required for conversion of homocysteine to methionine) and who have LOH at the methionine synthase (or other) gene locus. In such patients an allele specific inhibitor of MS directed to the sole allele present in cancer cells, coupled with methionine starvation or methioninase treatment, would selectively prevent tumor cells from responding to methionine deprivation. The provision of supplemental homocysteine, which could only be converted to methionine by the

normal cells, would provide a way to amplify the differential toxicity to cancer cells. Also, the methionine analog ethionine has been shown to potentiate the effects of methionine starvation. (Poirson-Bichat, F., et al., Growth of methionine-dependent human prostate cancer (PC-3) is inhibited by ethionine combined with methionine starvation. Br. J. Cancer 75: 1605-1612.) Ethionine or similar agents could be used in conjunction with an allele specific inhibitor of methionine synthesis.

5

10

15

20

25

An alternative approach to allele specific therapy of cancer cells with LOH would be to target the amino acid transport system for methionine in patients heterozygous for this protein and in whom only one allele is present in cancer tissue as a result of LOH. This would result in selective methionine starvation for cancer cells. Allele specific transport inhibition could be combined with methionine starvation or methioninase treatment to enhance the cytotoxic effect.

The Methionine Synthase gene maps to chromosome 1q43, a region subject to LOH in several cancers

The MS gene has been mapped to chromosome 1q43 by fluoresence in situ hybridization. The q43 region of chromosome 1 is subject to frequent LOH particularly in colon, head and neck, ovarian and liver cancers, where LOH frequencies vary from 11 to 39%. LOH at 1q43 has also been reported in cervix, pancreas, stomach and testis cancers. Several other cancer types have not yet been well studied for LOH in this region.

Other amino acid biosynthetic enzymes are candidates for allele specific inhibition

It will be evident to one skilled in the art that strategies similar to those described above for asparagine (an essential amino acid) and methionine (a non-essential amino acid) could be undertaken for other amino acid biosynthetic enzymes. For example,

232/116

L-glutaminase has also been shown to have antiproliferative effects on mammalian cell growth. Allele specific blockade of glutamine synthesis in heterozygous patients with LOH for genes essential for glutamine synthesis could be the basis of a cancer specific therapy.

5

Example 47. Methylthioadenosine phosphorylase (MTAP).

Variagenics Target Gene

10

Methylthioadenosine phosphorylase can convert methylthioadenosine to methionine, an essential amino acid

15

Cells require a continuous supply of amino acids for protein biosynthesis. L-methionine is one of ten essential amino acids. Consequently dividing cells must obtain methionine from serum via amino acid transporter (the only source besides protein catabolism or conversion of L-homocysteine). Alterations in the nutritional environment of growing cells that result in a decreased extracellular concentration of essential amino acids such as methionine cause arrested cell growth and may result in cell death. Cancer cells are particularly sensitive to methionine deprivation. (Tan, Y., et al., Anticancer Efficacy of Methioninase in vivo. *Anticancer Research* 16: 3931-3936.)

20

The cellular requirement for methionine can be bypassed by conversion of L-homocysteine to methionine as discussed above. An alternative pathway for methionine synthesis is conversion of 5'-methylthioadenosine (5'-MTA) via the action of 5'-MTA phosphorylase (MTAP). (Tisdale, M.J., Methionine Synthesis from 5'-methylthioadenosine by Tumor Cells. *Biochemical Pharmacology* 32: 2915-2920.) In tissue culture experiments low concentrations of 5'-MTA can substitute for

25

322

232/116

methionine in some cell lines. Thus 5'-MTA can rescue cells from methionine deprivation.

5

10

15

20

25

It occured to the inventors that allele specific inhibition of MTAP in cancer patients heterozygous for MTAP and whose cancer cells have only one allele of MTAP as a consequence of LOH, in combination with methionine deprivation (methionine starvation or L-methioninase treatment) and dietary supplementation with 5'-methylthioadenosine would provide a source of convertible methionine substrate selectively useful to normal cells. Tumor cells would have no source of methionine, being unable to convert the 5'-methylthioadenosine, and hence would be selectively poisoned. This therapeutic strategy would not necessarily require an allele specific inhibitor as *all copies* of MTAP are deleted in some cancers. Such cancers should be differentially poisoned vis a vis normal cells by methionine deprivation in the presence of 5'-methylthioadenosine.

The MTAP gene maps to 9p21, a region frequently subject to LOH in many cancers

The MTAP gene has been mapped to chromosome 9p21 by physical techniques (pulsed field gel electrophoresis and yeast artificial chromosome mapping). The gene lies near the cyclin dependent kinase inhibitors p16 and p15 which are frequently reduced to one or zero copies in cancer cells. (Nobori, et al., Genomic cloning of methylthioadenosine phosphorylase: a purine metabolic enzyme deficient in multiple different cancers. *Proc. Natl. Acad. Sci. U.S.A.* 93: 6203-6208.) The p21 region of chromosome 9 is subject to frequent LOH particularly in cancers of the bladder, breast, esophagus, head and neck, kidney, lung, melanoma and ovary. The frequency of LOH in these cancers ranges from 20% to nearly 100%.

323 232/116

Example 48. DNA dependent protein kinase (DNA-PK) and associated factors. Variagenics Target Genes

DNA dependent protein kinase is conditionally essential

5

Cells exposed to ionizing radiation, such as gamma radiation, are damaged by base modifications and DNA strand breaks. Double strand DNA breaks are among the most lethal form of radiation damage; one such break, if unrepaired, can be cell lethal. Four complementation groups of mammalian cell mutants that are defective in repair of double strand (ds) breaks have been identified. All four complementation groups are hypersensitive to ionizing radiation. The loci for three of these groups have been shown to encode components of DNA-dependent protein kinase (DNA-PK). The fourth group is deficient in the gene encoding XRCC4, a factor that associates with and stimulates DNA Ligase IV. Ligation of ds breaks by DNA ligase IV in a cell free system in increased 7-8 fold by co-expression of XRCC4.

15

20

10

DNA-PK is a multiprotein complex with a DNA binding regulatory subunit, the Ku heterodimer [Ku70 (XRCC6) and Ku80, also referred to as Ku86 (XRCC5)], and a catalytic subunit, DNA-PKcs (probably XRCC7), that is activated by the regulatory subunit upon binding to DNA ds ends, with consequent expression of serine/threonine kinase activity resulting in phosphorylation of a variety of DNA binding proteins. A fourth protein called KARP-1 is expressed from the Ku80/86 locus and is also implicated in DNA-PK function.

25

Cells lacking any of the components of DNA-PK are exquisitely sensitive to gamma irradation. This has been demonstrated directly in mice with targeted disruption of the Ku80/86 and DNA-PKcs genes. The Ku80/86 deficient mice were also sensitive to methyl methane sulfonate, a DNA alkylating agent that induces single strand breaks and to etoposide, a topoisomerase II inhibitor. Thus the components of DNA-PK can

324 232/116

also be important for repair of a variety of chemically induced DNA lesions as well as ionizing radiation.

5

10

15

20

In a cancer patient with two alternative alleles for a component of DNA-PK and LOH at the heterozygous locus, an allele specific inhibitory drug could be used to sensitize cancer cells to the action of ds break inducing treatments. Such a drug could be used to treat cancer patients constitutionally heterozygous for two normal alleles at any of the DNA-PK loci in whom LOH had rendered cancer cells hemizygous or homozygous for one allele. Treatment would consist in the administration of the appropriate allele specific inhibitor plus a ds break inducing agent or procedure. The tumor cells would be unable to effectively repair ds breaks, while the uninhibited allele in normal cells would be able to function. Alternatively, patients heterozygous for functional and defective copies of genes required for repair of strand breaks, and in whom LOH resulted in loss of the functional allele, could be treated by a strand break inducing procedure without the necessity for an allele specific inhibitor. Identification of such patients would require a test for heterozygosity at the target locus and a test for LOH which could show which allele is deleted in cancer cells. Such an approach would be expected to identify patients likely to respond well to strand breaking agents or procedures (exposure to ionizing radiation) even though they might have cancers not traditionally treated with such measures.

The genes encoding constituents of DNA-PK map to chromosomes frequently subject to LOH in different cancers

The DNA-PKcs gene has been mapped to 8q11, the Ku80/86 gene to 2q11-q13 and the Ku70 gene to 22q11-q13. All three regions are subject to LOH in different cancers. LOH on 2q has been reported in lung ovary and cervical cancers at frequencies ranging from 11% to 39%. LOH for 8q has been reported in cervix, head and neck, kidney, lung, ovary, prostate and testis cancers at frequencies ranging from 20% to 50% of

232/116

cancers. LOH on 22q has been reported in brain, breast colon, head and neck, lung, ovary, pediatric and stomach cancers at frequencies ranging from 10 to 76%. Several other cancer types have not yet been well studied for LOH affecting either region.

Other proteins required for repair of DNA strand breaks are also candidates for allele specific therapy of cancer

5

10

15

20

25

It will be evident to one skilled in the art that strategies similar to those described above for DNA-PK could be undertaken for other proteins required for repair of DNA strand breaks. For a recent review of such proteins see: Zdzienicka, M.Z., Mammalian mutants defective in the response to ionizing radiation-induced DNA damage. Mutation Research 336: 203-213, 1995; Thompson, L.H. and P.A. Jeggo, Nomenclature of human genes involved in ionizing radiation sensitivity. Mutation Research 337: 131-134, 1995; Thacker, J. and R.E. Wilkinson, The gentic basis of cellular recovery from radiation damage: response of the radiosensitive irs lines to lowdose rate irradiation. Radiation Research 144: 294-300, 1995. Two other syndromes with hypersensitivity to X-rays are Diamond-Blackfan anemia and aplastic anemia (Diemen, P.C., X-ray-sensitivity of lymphocytes of aplastic- and Diamond-Blackfananemia patients as detected by conventional cytogentic and chromosome painting techniques. Mutation Resarch 373: 225-235, 1997). Recently evidence of several other genes responsible for DNA double strand break repair has been described. (Nicolas, N., Finnie, N.J., et al., Eur. J. Immunol. 26:1118-1122, 1996.) The above genes which, when defective, sensitize cells to toxic effects of DNA strand breaking agents would be amenable to the therapeutic strategy outlined above for the DNA-PK genes. Specifically, in a patient with two alternative alleles for such a gene and LOH at the relevant locus, an allele specific drug could be used to sensitize cancer cells to the action of strand breaking agents. Such drugs could then be used to treat cancer patients constitutionally heterozygous for two normal alleles at the relevant locus, in whom LOH had rendered cancer cells hemizygous or homozygous for one allele.

Treatment would consist in the administration of the appropriate allele specific inhibitor plus a strand breaking agent or treatment to induce damage in all cells. Cancer cells (but not normal cells) would be rendered unable to respond by inhibition of expression of the relevant repair gene.

5

Alternatively, patients heterozygous for functional and defective copies of genes required for repair of strand breaks, and in whom LOH resulted in loss of the functional allele, could be treated by a strand break inducing procedure without the necessity for an allele specific inhibitor. Identification of such patients would require a test for heterozygosity at the target locus and a test for LOH which could show which allele is deleted in cancer cells. Such an approach would be expected to identify patients likely to respond well to strand breaking agents or procedures (exposure to ionizing radiation) even though they might have cancers not traditionally treated with such measures.

15

10

Example 49. Ataxia Telangiectasia Mutated (ATM) and c-Abl Variagenics Target Gene _____

20

The Ataxia Telangiectasia gene is essential for cell growth or survival in the presence of ionizing radiation or DNA damaging molecules

25

In order for cells to survive or proliferate in the presence of ionizing radiation (IR) or radiomimetic chemicals it is necessary that they are capable of efficiently repairing IR induced damage. Cells contain proteins necessary for such repair. One way such proteins can be identified is by their absence in specific patients who are particularly susceptible to the toxic effects of IR.

10

15

20

25

Ataxia Telangiectasia (AT) is a genetically transmitted autosomal recessive disorder characterized by variable degrees of immunodeficiency, telagiectasia (small blood vessels growing near the surface of the skin or eye), cerebellar ataxia (loss of balance due to abnormal development of the cerebellum) and increased sensitivity to both ionizing radiation and radiomimetic drugs, including bleomycin; AT cells are killed by lower doses of ionizing radiation or radiomimetic drugs than normal cells. Further, heterozygotes for mutant and normal AT alleles have radiation sensitivity close to that of homozygous normals. Therefore cancer cells from individuals heterozygous for null alleles of the AT gene (called ATM) should be highly susceptible to radiation therapy when only the deficient AT allele remains in cancer cells due to LOH, compared to normal cells from the same patients. Such patients could be treated by a DNA damage inducing procedure without the necessity for an allele specific inhibitor. Identification of such patients would require a test for heterozygosity at the target locus and a test for LOH which could show which allele is deleted in cancer cells. Such an approach would be expected to identify patients likely to respond well to strand breaking agents or procedures (such as exposure to ionizing radiation) even though they might have cancers not traditionally treated with such measures. In a related aspect, this approach is applicable to heterozygotes for other genes associated with ATM-mediated radiosensitivity. One such protein is the c-Abl protein tyrosine kinase, which binds to the ATM protein and regulates its function. c-Abl is known to be important in the stress response to ionizing radiation. One of its functions is activation of stress activated protein kinases (SAPKs) after irradiation or exposure to alkylating agents such as cis-platinum or mitomycin C, a response that is defective in ATM cells. Correction of the SAPK activation defect in ATM cells by non-mutant ATM cDNA suggests that the ATM - c-Abl interaction is necessary for the DNA damage response. (Kharbanda, S., et al. Nature 376: 785-788, 1995.)

In a cancer patient with two alternative functional alleles for a component of ATM and LOH at the ATM locus, an allele specific inhibitory drug could be used to sensitize

cancer cells to the action of DNA damage inducing treatments such as ionizing radiation or radiomimetic drugs. Such an allele specific drug could be used to treat cancer patients constitutionally heterozygous for two normal ATM alleles in whom LOH had rendered cancer cells hemizygous or homozygous for one allele. Treatment would consist of the administration of the appropriate allele specific inhibitor plus a DNA damage inducing treatment or procedure. The tumor cells would be unable to effectively the DNA damage, while the uninhibited allele in normal cells would be able to function. A similar approach could be taken to

The ATM gene is polymorphic

5

10

15

20

25

The ATM cDNA is 9.58 kb. Several likely polymorphisms have been identified, although population studies have not yet been performed to determine allele frequencies. One of the reported polymorphisms, an ATG to ATA change in codon 847, results in a methionine vs. isoleucine difference. Thus ATM is potentially targetable at the DNA, RNA and protein levels. It is likely that additional variances will be identified with broader population surveys and computational variance detection.

The ATM gene maps to chromosome 11q23 and the c-Abl gene maps to 9q34.1, two regions of high frequency LOH in different cancer types

Chromosome 9q34 is lost in a high fraction of bladder, esophagus, ovary, head & neck and testis cancers (17 - 76%) and in a lesser fraction of breast, liver and prostate cancers and leukemias. Chromosome 11q23 is lost in brain, cervix, esophagus, breast, kidney, colon, stomach, head & neck and lung cancers at frequencies ranging from 16% to 100%.

Other proteins required for repair of DNA damage are also candidates for allele specific therapy of cancer

329 232/116

It will be evident to one skilled in the art that strategies similar to those described above for ATM and c-Abl could be undertaken for other proteins required for the stress response to DNA damaging agents, such as other stress activated protein kinases or downstream effector proteins.

330

232/116

Methylguanine Methyltransferase (MGMT) Gene VARIA 1534

The methylguanine methyltransferase gene is essential for cell growth or survival in the presence of alkylating agents

Methylguanine methyltransferase (MGMT) is a suicide protein that repairs alkylating agent damage, specifically alkylation of the ⁶O position of guanine. Alkyl groups are covalently bound to an active site cysteine (residue 145) of MGMT, thereby irreversibly inactivating the protein. ⁶O-benzylguanine is an analog inhibitor of MGMT that, by inactivating MGMT, renders tumor cells more sensitive to the toxic effects of methylating and chloroethylating agents. MGMT is thus a conditionally essential gene in the presence of such drugs. ⁶O-benzylguanine is being developed as a chemosensitizing agent.

15

20

10

5

In a cancer patient with two alternative functional MGMT alleles an allele specific inhibitory drug could be used to sensitize cancer cells to the action of alkylating agents. Such an allele specific drug could be used to treat cancer patients constitutionally heterozygous for two normal MGMT alleles in whom LOH had rendered cancer cells hemizygous or homozygous for one allele. Treatment would consist of the administration of the appropriate allele specific inhibitor plus an alkylating agent. The tumor cells would be unable to effectively repair the alkylating agent induced DNA damage, while the uninhibited allele in normal cells would be able to function.

25 The MGMT gene is polymorphic

Several variances have been reported in human MGMT, or discovered by Variagenics, including three protein polymorphisms. There is a silent C/T variance at position 255 (11% heterozygotes among 36 individuals surveyed), another C/T variance at nt. 346

232/116

which results in a L84F amino acid variance (5% heterozygotes), an A/G variance at nt. 523 which results in a I143V amino acid variance (24% heterozygotes). A variance has been reported in Japanese at codon 160, GGA vs. AGA, converting glycine to arginine. 15% of the population studied were heterozygotes.

5

The alteration of glycine 160 to arginine reduced the inactivation by O6-benzylguanine with an approximately 20 fold increase in the IC50 concentration. These results demonstrate variance-specific effects of a small molecule, O6-benzylguanine, on normal (non-mutant) alleles of the conditionally essential MGMT gene.

10

Administration of O6 benzylguanine to patients who are heterozygous for the residue 160 gly/arg variance in their normal cells, and contain only the form of the gene with a glycine residue at position 160 in their cancer cells, together with methylating or chloroethylating agents for chemotherapy, will be specifically toxic to cancer cells without increasing toxicity to normal cells.

15

20

References

- 1. Imai, Y, Carcinogenesis (1995), 16:2441-24445
- 2. Edara, S. (1996) Resistance of the human O6-alkylguanine-DNA alkyltransferase containing arginine at codon 160 to inactivation by O6-benzylguanine. *Cancer Research* 56, 5571-5575.

25

All patents and publications mentioned in the specification are indicative of the levels of skill of those skilled in the art to which the invention pertains. All references cited in this disclosure are incorporated by reference to the same extent as if each reference had been incorporated by reference in its entirety individually.

One skilled in the art would readily appreciate that the present invention is well

adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The groups of genes and the particular genes described herein as presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art, which are encompassed within the spirit of the invention, are defined by the scope of the claims.

5

10

15

20

25

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. For example, those skilled in the art will readily recognize that the methods and inhibitors can utilize a variety of different target genes within the groups described. Thus, such additional embodiments are within the scope of the present invention and the following claims.

The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims.

333

232/116

In addition, where features or aspects of the invention are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush group or other group.

5

Thus, additional embodiments are within the scope of the invention and within the following claims.

CLAIMS

What we claim is:

5

1. A method for identifying an inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on a gene vital for cell growth or viability, and wherein said gene is subject to loss of heterozygosity in a cancer, said method comprising the steps of:

10

(a) determining at least two alleles of a said gene, wherein said gene encodes a product required for cell proliferation;

(b) testing a potential allele specific inhibitor to determine whether said potential allele specific inhibitor is active on at least one but less than all of said alleles;

wherein inhibition of expression of at least one but less than all of said alleles or reduction of the level of activity of a product of at least one but less than all of said alleles in the presence of said potential allele specific inhibitor is indicative that said potential allele specific inhibitor is a said inhibitor.

15

2. A method for identifying an inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on a gene vital for cell growth or viability, and wherein said gene is subject to loss of heterozygosity in a cancer, said method comprising the steps of:

20

(a) determining at least two alleles of a said gene, wherein said gene encodes a product required to maintain inorganic ions and vitamins at levels compatible with cell growth or survival;

25

(b) testing a potential allele specific inhibitor to determine whether said potential allele specific inhibitor is active on at least one but less than all of said alleles;

wherein inhibition of expression of at least one but less than all of said alleles or reduction of the level of activity of a product of at least one but less than all of

10

15

20

25

said alleles in the presence of said potential allele specific inhibitor is indicative that said potential allele specific inhibitor is a said inhibitor.

- 3. A method for identifying an inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on a gene vital for cell growth or viability, and wherein said gene is subject to loss of heterozygosity in a cancer, said method comprising the steps of:
- (a) determining at least two alleles of a said gene, wherein said gene encodes a product required to maintain organic compounds at levels compatible with cell growth or survival;
- (b) testing a potential allele specific inhibitor to determine whether said potential allele specific inhibitor is active on at least one but less than all of said alleles;

wherein inhibition of expression of at least one but less than all of said alleles or reduction of the level of activity of a product of at least one but less than all of said alleles in the presence of said potential allele specific inhibitor is indicative that said potential allele specific inhibitor is a said inhibitor.

- 4. A method for identifying an inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on a gene vital for cell growth or viability, and wherein said gene is subject to loss of heterozygosity in a cancer, said method comprising the steps of:
- (a) determining at least two alleles of a said gene, wherein said gene encodes a product required to maintain cellular proteins at levels compatible with cell growth or survival;
- (b) testing a potential allele specific inhibitor to determine whether said potential allele specific inhibitor is active on at least one but less than all of said alleles;

wherein inhibition of expression of at least one but less than all of said alleles

PCT/US98/05419

232/116

or reduction of the level of activity of a product of at least one but less than all of said alleles in the presence of said potential allele specific inhibitor is indicative that said potential allele specific inhibitor is a said inhibitor.

5

WO 98/41648

5. A method for identifying an inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on a gene vital for cell growth or viability, and wherein said gene is subject to loss of heterozygosity in a cancer, said method comprising the steps of:

10

- (a) determining at least two alleles of a said gene, wherein said gene encodes a product required to maintain cellular nucleotides at levels compatible with cell growth or survival;
- (b) testing a potential allele specific inhibitor to determine whether said potential allele specific inhibitor is active on at least one but less than all of said alleles;

15

wherein inhibition of expression of at least one but less than all of said alleles or reduction of the level of activity of a product of at least one but less than all of said alleles in the presence of said potential allele specific inhibitor is indicative that said potential allele specific inhibitor is a said inhibitor.

20

6. A method for identifying an inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on a gene vital for cell growth or viability, and wherein said gene is subject to loss of heterozygosity in a cancer, said method comprising the steps of:

25

- (a) determining at least two alleles of a said gene, wherein said gene encodes a product required to maintain the integrity and function of cellular and subcellular structures;
- (b) testing a potential allele specific inhibitor to determine whether said potential allele specific inhibitor is active on at least one but less than all of said alleles;

wherein inhibition of expression of at least one but less than all of said alleles or reduction of the level of activity of a product of at least one but less than all of said alleles in the presence of said potential allele specific inhibitor is indicative that said potential allele specific inhibitor is a said inhibitor.

5

7. A method for identifying an inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on a gene vital for cell growth or viability, and wherein said gene is subject to loss of heterozygosity in a cancer, said method comprising the steps of:

10

- (a) determining at least two alleles of a said gene, wherein said gene is located on a high frequency LOH chromosomal region;
- (b) testing a potential allele specific inhibitor to determine whether said potential allele specific inhibitor is active on at least one but less than all of said alleles;

15

wherein inhibition of expression of at least one but less than all of said alleles or reduction of the level of activity of a product of at least one but less than all of said alleles in the presence of said potential allele specific inhibitor is indicative that said potential allele specific inhibitor is a said inhibitor.

20

8. The method of claim 7, wherein said gene is located on a chromosomal arm which has a frequency of allele loss of at least 15% in a cancer.

25

The method of claim 7, wherein said gene is located in proximity to a chromosomal marker which undergoes LOH at a frequency of at least 10% in a cancer.

9.

10. The method of claim 7, wherein said gene is located in proximity to a tumor suppressor gene which undergoes LOH at a frequency of at least 10% in a cancer.

WO 98/41648

5

10

15

20

25

11. A method for identifying an inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on a gene vital for cell growth or viability, and wherein said gene is subject to loss of heterozygosity in a cancer, said method comprising the steps of:

(a) determining at least two alleles of a said gene, wherein said gene has at least two sequence variances which occur at frequences such that at least 10% of a population is heterozygous for said gene;

(b) testing a potential allele specific inhibitor to determine whether said potential allele specific inhibitor is active on at least one but less than all of said alleles;

wherein inhibition of expression of at least one but less than all of said alleles or reduction of the level of activity of a product of at least one but less than all of said alleles in the presence of said potential allele specific inhibitor is indicative that said potential allele specific inhibitor is a said inhibitor.

- 12. The method of claim 11, wherein said gene is located on a high frequency LOH chromosomal region.
- 13. An inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on an allelic form of a gene vital for cell viability or cell growth, wherein said gene encodes a product required for cell proliferation, said gene has at least two alternative alleles in a population, and

wherein said inhibitor targets at least one but less than all of said alternative alleles.

14. An inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on an allelic form of a gene vital for cell viability or cell growth, wherein said gene encodes a product required to maintain inorganic ions and vitamins at levels compatible with cell growth or survival, said gene has at least two alternative

alleles in a population, and

wherein said inhibitor targets at least one but less than all of said alternative alleles.

5

15. An inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on an allelic form of a gene vital for cell viability or cell growth, wherein said gene encodes a product required to maintain organic compounds at levels compatible with cell growth or survival, said gene has at least two alternative alleles in a population, and

wherein said inhibitor targets at least one but less than all of said alternative alleles.

15

10

16. An inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on an allelic form of a gene vital for cell viability or cell growth, wherein said gene encodes a product required to maintain cellular proteins at levels compatible with cell growth or survival, said gene has at least two alternative alleles in a population, and

20

wherein said inhibitor targets at least one but less than all of said alternative alleles.

25

17. An inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on an allelic form of a gene vital for cell viability or cell growth, wherein said gene encodes a product required to maintain cellular nucleotides at levels compatible with cell growth or survival, said gene has at least two alternative alleles in a population, and

wherein said inhibitor targets at least one but less than all of said alternative alleles.

10

15

20

25

18. An inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on an allelic form of a gene vital for cell viability or cell growth, wherein said gene encodes a product required to maintain the integrity and function of cellular and subcellular structures, said gene has at least two alternative alleles in a population, and

wherein said inhibitor targets at least one but less than all of said alternative alleles.

19. An inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on an allelic form of a gene vital for cell viability or cell growth, wherein said gene is located on a high frequency LOH chromosomal arm region, said gene has at least two alternative alleles in a population, and

wherein said inhibitor targets at least one but less than all of said alternative alleles.

20. An inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on an allelic form of a gene vital for cell viability or cell growth, wherein said gene has at least two sequence variances which occur at frequences such that at least 10% of a population is heterozygous for said gene, said gene has at least two alternative alleles in a population, and

wherein said inhibitor targets at least one but less than all of said alternative alleles.

21. A pharmaceutical composition, comprising

at least one allele specific inhibitor targeting at least one but less than all allelic forms of an essential gene in a population, wherein said gene encodes a product required for cell proliferation; and

a pharmaceutically acceptable carrier or excipient.

10

15

20

25

22. A pharmaceutical composition, comprising

at least one allele specific inhibitor targeting at least one but less than all allelic forms of an essential gene in a population, wherein said gene encodes a product required to maintain inorganic ions and vitamins at levels compatible with cell growth or survival; and

a pharmaceutically acceptable carrier or excipient.

23. A pharmaceutical composition, comprising

at least one allele specific inhibitor targeting at least one but less than all allelic forms of an essential gene in a population, wherein said gene encodes a product required to maintain organic compounds at levels compatible with cell growth or survival; and

a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition, comprising

at least one allele specific inhibitor targeting at least one but less than all allelic forms of an essential gene in a population, wherein said gene encodes a product required to maintain cellular proteins at levels compatible with cell growth or survival; and

a pharmaceutically acceptable carrier or excipient.

25. A pharmaceutical composition, comprising

at least one allele specific inhibitor targeting at least one but less than all allelic forms of an essential gene in a population, wherein said gene encodes a product required to maintain cellular nucleotides at levels compatible with cell growth or survival; and

a pharmaceutically acceptable carrier or excipient.

15

20

25

26. A pharmaceutical composition, comprising

at least one allele specific inhibitor targeting at least one but less than all allelic forms of an essential gene in a population, wherein said gene encodes a product required to maintain the integrity and function of cellular and subcellular structures; and

a pharmaceutically acceptable carrier or excipient.

10 27. A pharmaceutical composition, comprising

at least one allele specific inhibitor targeting at least one but less than all allelic forms of an essential gene in a population, wherein said gene is located on a high frequency LOH chromosomal arm region; and

a pharmaceutically acceptable carrier or excipient.

28. A pharmaceutical composition, comprising

at least one allele specific inhibitor targeting at least one but less than all allelic forms of an essential gene in a population, wherein said gene has at least two sequence variances which occur at frequences such that at least 10% of a population is heterozygous for said gene; and

a pharmaceutically acceptable carrier or excipient.

- 29. A method for producing an inhibitor potentially useful for cancer treatment, wherein said inhibitor is active on at least one but less than all alternative alleles of a gene having at least two alternative alleles, comprising the steps of:
- (a) identifying a gene vital to cell viability or cell growth that has alternative allelic forms in a noncancerous cell, wherein one of said alternative allelic forms is deleted in a cancer cell, and wherein said gene encodes a product required for cell proliferation;

WO 98/41648

5

10

15

20

- (b) screening to identify an inhibitor which inhibits said at least one but less than all of said at least two alternative alleles; and
- (c) synthesizing said inhibitor in an amount sufficient to produce a therapeutic effect when administered to a patient suffering from a cancer in which cancerous cells have only the allele of said gene inhibited by said inhibitor and in whom normal cells are heterozygous for said gene.
- 30. A method for producing an inhibitor potentially useful for cancer treatment, wherein said inhibitor is active on at least one but less than all alternative alleles of a gene having at least two alternative alleles, comprising the steps of:
- (a) identifying a gene vital to cell viability or cell growth that has alternative allelic forms in a noncancerous cell, wherein one of said alternative allelic forms is deleted in a cancer cell, and wherein said gene encodes a product required to maintain inorganic ions and vitamins at levels compatible with cell growth or survival;
- (b) screening to identify an inhibitor which inhibits said at least one but less than all of said at least two alternative alleles; and
- (c) synthesizing said inhibitor in an amount sufficient to produce a therapeutic effect when administered to a patient suffering from a cancer in which cancerous cells have only the allele of said gene inhibited by said inhibitor and in whom normal cells are heterozygous for said gene.
- 31. A method for producing an inhibitor potentially useful for cancer treatment, wherein said inhibitor is active on at least one but less than all alternative alleles of a gene having at least two alternative alleles, comprising the steps of:
- (a) identifying a gene vital to cell viability or cell growth that has alternative allelic forms in a noncancerous cell, wherein one of said alternative allelic forms is deleted in a cancer cell, and wherein said gene encodes a product required to maintain organic compounds at levels compatible with cell growth or survival:

WO 98/41648

5

10

15

20

- (b) screening to identify an inhibitor which inhibits said at least one but less than all of said at least two alternative alleles; and
- (c) synthesizing said inhibitor in an amount sufficient to produce a therapeutic effect when administered to a patient suffering from a cancer in which cancerous cells have only the allele of said gene inhibited by said inhibitor and in whom normal cells are heterozygous for said gene.
- 32. A method for producing an inhibitor potentially useful for cancer treatment, wherein said inhibitor is active on at least one but less than all alternative alleles of a gene having at least two alternative alleles, comprising the steps of:
- (a) identifying a gene vital to cell viability or cell growth that has alternative allelic forms in a noncancerous cell, wherein one of said alternative allelic forms is deleted in a cancer cell, and wherein said gene encodes a product required to maintain cellular proteins at levels compatible with cell growth or survival;
- (b) screening to identify an inhibitor which inhibits said at least one but less than all of said at least two alternative alleles; and
- (c) synthesizing said inhibitor in an amount sufficient to produce a therapeutic effect when administered to a patient suffering from a cancer in which cancerous cells have only the allele of said gene inhibited by said inhibitor and in whom normal cells are heterozygous for said gene.
- 33. A method for producing an inhibitor potentially useful for cancer treatment, wherein said inhibitor is active on at least one but less than all alternative alleles of a gene having at least two alternative alleles, comprising the steps of:
- (a) identifying a gene vital to cell viability or cell growth that has alternative allelic forms in a noncancerous cell, wherein one of said alternative allelic forms is deleted in a cancer cell, and wherein said gene encodes a product required to maintain cellular nucleotides at levels compatible with cell growth or survival;
 - (b) screening to identify an inhibitor which inhibits said at least one but less

10

15

20

25

than all of said at least two alternative alleles; and

- (c) synthesizing said inhibitor in an amount sufficient to produce a therapeutic effect when administered to a patient suffering from a cancer in which cancerous cells have only the allele of said gene inhibited by said inhibitor and in whom normal cells are heterozygous for said gene.
- 34. A method for producing an inhibitor potentially useful for cancer treatment, wherein said inhibitor is active on at least one but less than all alternative alleles of a gene having at least two alternative alleles, comprising the steps of:
- (a) identifying a gene vital to cell viability or cell growth that has alternative allelic forms in a noncancerous cell, wherein one of said alternative allelic forms is deleted in a cancer cell, and wherein said gene encodes a product required to maintain the integrity and function of cellular and subcellular structures;
- (b) screening to identify an inhibitor which inhibits said at least one but less than all of said at least two alternative alleles; and
- (c) synthesizing said inhibitor in an amount sufficient to produce a therapeutic effect when administered to a patient suffering from a cancer in which cancerous cells have only the allele of said gene inhibited by said inhibitor and in whom normal cells are heterozygous for said gene.
- 35. A method for producing an inhibitor potentially useful for cancer treatment, wherein said inhibitor is active on at least one but less than all alternative alleles of a gene having at least two alternative alleles, comprising the steps of:
- (a) identifying a gene vital to cell viability or cell growth that has alternative allelic forms in a noncancerous cell, wherein one of said alternative allelic forms is deleted in a cancer cell, and wherein said gene is located on a high frequency LOH chromosomal arm region;
- (b) screening to identify an inhibitor which inhibits said at least one but less than all of said at least two alternative alleles; and

(c) synthesizing said inhibitor in an amount sufficient to produce a therapeutic effect when administered to a patient suffering from a cancer in which cancerous cells have only the allele of said gene inhibited by said inhibitor and in whom normal cells are heterozygous for said gene.

5

36. A method for producing an inhibitor potentially useful for cancer treatment, wherein said inhibitor is active on at least one but less than all alternative alleles of a gene having at least two alternative alleles, comprising the steps of:

10

(a) identifying a gene vital to cell viability or cell growth that has alternative allelic forms in a noncancerous cell, wherein one of said alternative allelic forms is deleted in a cancer cell, and wherein said gene has at least two sequence variances which occur at frequences such that at least 10% of a population is heterozygous for said gene;

15

than all of said at least two alternative alleles; and

(c) synthesizing said inhibitor in an amount sufficient to produce a therapeutic effect when administered to a patient suffering from a cancer in which cancerous cells have only the allele of said gene inhibited by said inhibitor and in whom normal cells are heterozygous for said gene.

(b) screening to identify an inhibitor which inhibits said at least one but less

20

37. A method for preventing the development of cancer in a patient having a precancerous condition, comprising the steps of:

25

a. administering to said patient a therapeutic amount of a first allele specific inhibitor targeted to an allele of a first essential gene present in cells of said precancerous condition, wherein the normal somatic cells of said patient are heterozygous for said first gene, said inhibitor is active on at least one but less than all allelic forms of said gene present in a population and targets only one allelic form present in said normal somatic cells, and said first gene encodes a product required for cell proliferation; and

wherein cells of said precancerous condition have undergone LOH of said first gene.

38. The method of claim 37, wherein the cells of said precancerous condition are not clonal from a single cell, further comprising the step of:

b. serially administering to said patient at least one additional allele specific inhibitor, wherein each of said at least one additional allele specific inhibitors targets a different allele of an essential gene than is targeted by said first allele specific inhibitor, wherein said different allele may be a different allele of said first gene or an allele of a different essential gene, and wherein said patient is heterozygous for each targeted essential gene and each targeted essential gene has undergone LOH in cells of said precancerous condition.

15

10

5

39. A method for preventing the development of cancer in a patient having a precancerous condition, comprising the steps of:

a. administering to said patient a therapeutic amount of a first allele specific

20

inhibitor targeted to an allele of a first essential gene present in cells of said precancerous condition, wherein the normal somatic cells of said patient are heterozygous for said first gene, said inhibitor is active on at least one but less than all allelic forms of said gene present in a population and targets only one allelic form present in said normal somatic cells, and said first gene encodes a product required to maintain inorganic ions and vitamins at levels compatible with cell growth or

25

survival; and

wherein cells of said precancerous condition have undergone LOH of said first gene.

40. The method of claim 39, wherein the cells of said precancerous condition are

10

15

20

25

not clonal from a single cell, further comprising the step of:

b. serially administering to said patient at least one additional allele specific inhibitor, wherein each of said at least one additional allele specific inhibitors targets a different allele of an essential gene than is targeted by said first allele specific inhibitor, wherein said different allele may be a different allele of said first gene or an allele of a different essential gene, and wherein said patient is heterozygous for each targeted essential gene and each targeted essential gene has undergone LOH in cells of said precancerous condition.

- 41. A method for preventing the development of cancer in a patient having a precancerous condition, comprising the steps of:
- a. administering to said patient a therapeutic amount of a first allele specific inhibitor targeted to an allele of a first essential gene present in cells of said precancerous condition, wherein the normal somatic cells of said patient are heterozygous for said first gene, said inhibitor is active on at least one but less than all allelic forms of said gene present in a population and targets only one allelic form present in said normal somatic cells, and said first gene encodes a product required to maintain organic compounds at levels compatible with cell growth or survival; and

wherein cells of said precancerous condition have undergone LOH of said first gene.

- 42. The method of claim 41, wherein the cells of said precancerous condition are not clonal from a single cell, further comprising the step of:
- b. serially administering to said patient at least one additional allele specific inhibitor, wherein each of said at least one additional allele specific inhibitors targets a different allele of an essential gene than is targeted by said first allele specific inhibitor, wherein said different allele may be a different allele of said first gene or an allele of a different essential gene, and wherein said patient is heterozygous for each targeted essential gene and each targeted essential gene has undergone LOH in

WO 98/41648

cells of said precancerous condition.

43. A method for preventing the development of cancer in a patient having a precancerous condition, comprising the steps of:

5

a. administering to said patient a therapeutic amount of a first allele specific inhibitor targeted to an allele of a first essential gene present in cells of said precancerous condition, wherein the normal somatic cells of said patient are heterozygous for said first gene, said inhibitor is active on at least one but less than all allelic forms of said gene present in a population and targets only one allelic form present in said normal somatic cells, and said first gene encodes a product required to maintain cellular proteins at levels compatible with cell growth or survival; and

wherein cells of said precancerous condition have undergone LOH of said first gene.

15

10

44. The method of claim 43, wherein the cells of said precancerous condition are not clonal from a single cell, further comprising the step of:

20

b. serially administering to said patient at least one additional allele specific inhibitor, wherein each of said at least one additional allele specific inhibitors targets a different allele of an essential gene than is targeted by said first allele specific inhibitor, wherein said different allele may be a different allele of said first gene or an allele of a different essential gene, and wherein said patient is heterozygous for each targeted essential gene and each targeted essential gene has undergone LOH in cells of said precancerous condition.

- 45. A method for preventing the development of cancer in a patient having a precancerous condition, comprising the steps of:
- a. administering to said patient a therapeutic amount of a first allele specific inhibitor targeted to an allele of a first essential gene present in cells of said precancerous condition, wherein the normal somatic cells of said patient are

10

15

20

25

heterozygous for said first gene, said inhibitor is active on at least one but less than all allelic forms of said gene present in a population and targets only one allelic form present in said normal somatic cells, and said first gene encodes a product required to maintain cellular nucleotides at levels compatible with cell growth or survival; and

wherein cells of said precancerous condition have undergone LOH of said first gene.

- 46. The method of claim 45, wherein the cells of said precancerous condition are not clonal from a single cell, further comprising the step of:
- b. serially administering to said patient at least one additional allele specific inhibitor, wherein each of said at least one additional allele specific inhibitors targets a different allele of an essential gene than is targeted by said first allele specific inhibitor, wherein said different allele may be a different allele of said first gene or an allele of a different essential gene, and wherein said patient is heterozygous for each targeted essential gene and each targeted essential gene has undergone LOH in cells of said precancerous condition.
- 47. A method for preventing the development of cancer in a patient having a precancerous condition, comprising the steps of:
- a. administering to said patient a therapeutic amount of a first allele specific inhibitor targeted to an allele of a first essential gene present in cells of said precancerous condition, wherein the normal somatic cells of said patient are heterozygous for said first gene, said inhibitor is active on at least one but less than all allelic forms of said gene present in a population and targets only one allelic form present in said normal somatic cells, and said first gene encodes a product required to maintain the integrity and function of cellular and subcellular structures; and

wherein cells of said precancerous condition have undergone LOH of said first gene.

PCT/US98/05419

232/116

48. The method of claim 47, wherein the cells of said precancerous condition are not clonal from a single cell, further comprising the step of:

b. serially administering to said patient at least one additional allele specific inhibitor, wherein each of said at least one additional allele specific inhibitors targets a different allele of an essential gene than is targeted by said first allele specific inhibitor, wherein said different allele may be a different allele of said first gene or an allele of a different essential gene, and wherein said patient is heterozygous for each targeted essential gene and each targeted essential gene has undergone LOH in cells of said precancerous condition.

10

5

WO 98/41648

49. A method for preventing the development of cancer in a patient having a precancerous condition, comprising the steps of:

a. administering to said patient a therapeutic amount of a first allele specific inhibitor targeted to an allele of a first essential gene present in cells of said precancerous condition, wherein the normal somatic cells of said patient are heterozygous for said first gene, said inhibitor is active on at least one but less than all allelic forms of said gene present in a population and targets only one allelic form present in said normal somatic cells, and said first gene is located on a high frequency LOH chromosomal arm region; and

20

15

wherein cells of said precancerous condition have undergone LOH of said first gene.

50. The method of claim 49, wherein the cells of said precancerous condition are not clonal from a single cell, further comprising the step of:

25

b. serially administering to said patient at least one additional allele specific inhibitor, wherein each of said at least one additional allele specific inhibitors targets a different allele of an essential gene than is targeted by said first allele specific inhibitor, wherein said different allele may be a different allele of said first gene or an allele of a different essential gene, and wherein said patient is heterozygous for

PCT/US98/05419

232/116

WO 98/41648

5

10

15

20

25

352

each targeted essential gene and each targeted essential gene has undergone LOH in cells of said precancerous condition.

51. A method for preventing the development of cancer in a patient having a precancerous condition, comprising the steps of:

a. administering to said patient a therapeutic amount of a first allele specific inhibitor targeted to an allele of a first essential gene present in cells of said precancerous condition, wherein the normal somatic cells of said patient are heterozygous for said first gene, said inhibitor is active on at least one but less than all allelic forms of said gene present in a population and targets only one allelic form present in said normal somatic cells, and said first gene has at least two sequence variances which occur at frequences such that at least 10% of a population is heterozygous for said gene; and

wherein cells of said precancerous condition have undergone LOH of said first gene.

- 52. The method of claim 51, wherein the cells of said precancerous condition are not clonal from a single cell, further comprising the step of:
- b. serially administering to said patient at least one additional allele specific inhibitor, wherein each of said at least one additional allele specific inhibitors targets a different allele of an essential gene than is targeted by said first allele specific inhibitor, wherein said different allele may be a different allele of said first gene or an allele of a different essential gene, and wherein said patient is heterozygous for each targeted essential gene and each targeted essential gene has undergone LOH in cells of said precancerous condition.
- 53. A method for treating a patient suffering from a cancer, wherein said patient is heterozygous for a gene vital for cell growth or viability, comprising the step of: administering a therapeutic amount of an allele specific inhibitor active on at

least one but less than all allelic forms of said gene present in a population,

wherein said gene encodes a product required for cell proliferation, said allele specific inhibitor inhibits only one allelic form of said gene present in said patient, and said only one allelic form of said gene is present in cancer cells in said patient.

5

10

- 54. The method of claim 53, further comprising the steps of:
- (a) determining whether non-cancerous cells of said patient are heterozygous for a particular gene essential for cell growth or viability; or
- (b) determining whether cancerous cells of said patient have only one allele of said particular gene; or
 - (c) both (a) and (b).
- 55. A method for treating a patient suffering from a cancer, wherein said patient is heterozygous for a gene vital for cell growth or viability, comprising the step of:

administering a therapeutic amount of an allele specific inhibitor active on at least one but less than all allelic forms of said gene present in a population,

wherein said gene encodes a product required to maintain inorganic ions and vitamins at levels compatible with cell growth or survival, said allele specific inhibitor inhibits only one allelic form of said gene present in said patient, and said only one allelic form of said gene is present in cancer cells in said patient.

20

25

- 56. The method of claim 55, further comprising the steps of:
- (a) determining whether non-cancerous cells of said patient are heterozygous for a particular gene essential for cell growth or viability; or
- (b) determining whether cancerous cells of said patient have only one allele of said particular gene; or
 - (c) both (a) and (b).
- 57. A method for treating a patient suffering from a cancer, wherein said patient

354 232/116

PCT/US98/05419

is heterozygous for a gene vital for cell growth or viability, comprising the step of:
administering a therapeutic amount of an allele specific inhibitor active on at
least one but less than all allelic forms of said gene present in a population,

wherein said gene encodes a product required to maintain organic compounds at levels compatible with cell growth or survival, said allele specific inhibitor inhibits only one allelic form of said gene present in said patient, and said only one allelic form of said gene is present in cancer cells in said patient.

- 58. The method of claim 57, further comprising the steps of:
- (a) determining whether non-cancerous cells of said patient are heterozygous for a particular gene essential for cell growth or viability; or
- (b) determining whether cancerous cells of said patient have only one allele of said particular gene; or
 - (c) both (a) and (b).

15

WO 98/41648

5

10

20

25

59. A method for treating a patient suffering from a cancer, wherein said patient is heterozygous for a gene vital for cell growth or viability, comprising the step of: administering a therapeutic amount of an allele specific inhibitor active on at

least one but less than all allelic forms of said gene present in a population,

wherein said gene encodes a product required to maintain cellular proteins at levels compatible with cell growth or survival, said allele specific inhibitor inhibits only one allelic form of said gene present in said patient, and said only one allelic form of said gene is present in cancer cells in said patient.

- 60. The method of claim 59, further comprising the steps of:
- (a) determining whether non-cancerous cells of said patient are heterozygous for a particular gene essential for cell growth or viability; or
- (b) determining whether cancerous cells of said patient have only one allele of said particular gene; or

WO 98/41648 PCT/US98/05419

355 232/116

(c) both (a) and (b).

5

10

15

20

25

61. A method for treating a patient suffering from a cancer, wherein said patient is heterozygous for a gene vital for cell growth or viability, comprising the step of:

administering a therapeutic amount of an allele specific inhibitor active on at least one but less than all allelic forms of said gene present in a population,

wherein said gene encodes a product required to maintain cellular nucleotides at levels compatible with cell growth or survival, said allele specific inhibitor inhibits only one allelic form of said gene present in said patient, and said only one allelic form of said gene is present in cancer cells in said patient.

62. The method of claim 61, further comprising the steps of:

- (a) determining whether non-cancerous cells of said patient are heterozygous for a particular gene essential for cell growth or viability; or
- (b) determining whether cancerous cells of said patient have only one allele of said particular gene; or
 - (c) both (a) and (b).

63. A method for treating a patient suffering from a cancer, wherein said patient is heterozygous for a gene vital for cell growth or viability, comprising the step of:

administering a therapeutic amount of an allele specific inhibitor active on at least one but less than all allelic forms of said gene present in a population,

wherein said gene encodes a product required to maintain the integrity and function of cellular and subcellular structures, said allele specific inhibitor inhibits only one allelic form of said gene present in said patient, and said only one allelic form of said gene is present in cancer cells in said patient.

- 64. The method of claim 63, further comprising the steps of:
 - (a) determining whether non-cancerous cells of said patient are

232/116

heterozygous for a particular gene essential for cell growth or viability; or

- (b) determining whether cancerous cells of said patient have only one allele of said particular gene; or
 - (c) both (a) and (b).

5

65. A method for treating a patient suffering from a cancer, wherein said patient is heterozygous for a gene vital for cell growth or viability, comprising the step of: administering a therapeutic amount of an allele specific inhibitor active on at least one but less than all allelic forms of said gene present in a population,

10

wherein said gene is located on a high frequency LOH chromosomal arm region, said allele specific inhibitor inhibits only one allelic form of said gene present in said patient, and said only one allelic form of said gene is present in cancer cells in said patient.

15

- 66. The method of claim 65, further comprising the steps of:
- (a) determining whether non-cancerous cells of said patient are heterozygous for a particular gene essential for cell growth or viability; or
- (b) determining whether cancerous cells of said patient have only one allele of said particular gene; or
 - (c) both (a) and (b).

20

25

67. A method for treating a patient suffering from a cancer, wherein said patient is heterozygous for a gene vital for cell growth or viability, comprising the step of: administering a therapeutic amount of an allele specific inhibitor active on at

least one but less than all allelic forms of said gene present in a population,

wherein said gene has at least two sequence variances which occur at frequences such that at least 10% of a population is heterozygous for said gene, said allele specific inhibitor inhibits only one allelic form of said gene present in said patient, and said only one allelic form of said gene is present in cancer cells in said

patient.

5

15

20

25

- 68. The method of claim 67, further comprising the steps of:
- (a) determining whether non-cancerous cells of said patient are heterozygous for a particular gene essential for cell growth or viability; or
- (b) determining whether cancerous cells of said patient have only one allele of said particular gene; or
 - (c) both (a) and (b).
- 10 69. A method of inhibiting growth of a cell comprising the step of:

administering at least one inhibitor active on an allele of a gene vital for cell viability or growth,

wherein said gene encodes a product required for cell proliferation, and wherein said inhibitor is less active on at least one other allele of said gene.

70. A method of inhibiting growth of a cell comprising the step of:

administering at least one inhibitor active on an allele of a gene vital for cell viability or growth,

wherein said gene encodes a product required to maintain inorganic ions and vitamins at levels compatible with cell growth or survival, and wherein said inhibitor is less active on at least one other allele of said gene.

71. A method of inhibiting growth of a cell comprising the step of:

administering at least one inhibitor active on an allele of a gene vital for cell viability or growth,

wherein said gene encodes a product required to maintain organic compounds at levels compatible with cell growth or survival, and wherein said inhibitor is less active on at least one other allele of said gene.

10

15

20

25

232/116

72. A method of inhibiting growth of a cell comprising the step of:

administering at least one inhibitor active on an allele of a gene vital for cell viability or growth,

wherein said gene encodes a product required to maintain cellular proteins at levels compatible with cell growth or survival, and wherein said inhibitor is less active on at least one other allele of said gene.

73. A method of inhibiting growth of a cell comprising the step of:

administering at least one inhibitor active on an allele of a gene vital for cell viability or growth,

wherein said gene encodes a product required to maintain cellular nucleotides at levels compatible with cell growth or survival, and wherein said inhibitor is less active on at least one other allele of said gene.

74. A method of inhibiting growth of a cell comprising the step of:

administering at least one inhibitor active on an allele of a gene vital for cell viability or growth,

wherein said gene encodes a product required to maintain the integrity and function of cellular and subcellular structures, and wherein said inhibitor is less active on at least one other allele of said gene.

75. A method of inhibiting growth of a cell comprising the step of:

administering at least one inhibitor active on an allele of a gene vital for cell viability or growth,

wherein said gene is located on a high frequency LOH chromosomal arm region, and wherein said inhibitor is less active on at least one other allele of said gene.

76. A method of inhibiting growth of a cell comprising the step of:

10

15

20

25

administering at least one inhibitor active on an allele of a gene vital for cell viability or growth,

wherein said gene has at least two sequence variances which occur at frequences such that at least 10% of a population is heterozygous for said gene, and wherein said inhibitor is less active on at least one other allele of said gene.

77. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the step of:

identifying a patient heterozygous for a said gene encoding a product required for cell proliferation,

wherein if said patient is heterozygous for said gene, then said patient is a potential patient for said treatment.

78. The method of claim 77, further comprising the step of determining whether cancer cells in said patient contain only a single allele of said gene,

wherein if said cancer cells contain only a single allele of said gene, then said patient is a potential patient for said treatment.

79. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the step of:

determining whether cancer cells in said patient have undergone LOH of a said gene encoding a product required for cell proliferation,

wherein if said cells have undergone LOH of said gene, then said patient is a potential patient for said treatment.

80. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the step of:

5

identifying a patient heterozygous for a said gene encoding a product required to maintain inorganic ions and vitamins at levels compatible with cell growth or survival,

wherein if said patient is heterozygous for said gene, then said patient is a potential patient for said treatment.

10

81. The method of claim 80, further comprising the step of determining whether cancer cells in said patient contain only a single allele of said gene,

wherein if said cancer cells contain only a single allele of said gene, then said patient is a potential patient for said treatment.

15

82. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the step of:

20

determining whether cancer cells in said patient have undergone LOH of a said gene encoding a product required to maintain inorganic ions and vitamins at levels compatible with cell growth or survival,

wherein if said cells have undergone LOH of said gene, then said patient is a potential patient for said treatment.

25

83. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the steps of:

identifying a patient heterozygous for a said gene encoding a product required to maintain organic compounds at levels compatible with cell growth or survival;

wherein if said patient is heterozygous for said gene, then said patient is a potential patient for said treatment.

5

84. The method of claim 83, further comprising the step of determining whether cancer cells in said patient contain only a single allele of said gene,

wherein if said cancer cells contain only a single allele of said gene, then said patient is a potential patient for said treatment.

10

85. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the step of:

15

determining whether cancer cells in said patient have undergone LOH of a said gene encoding a product required to maintain organic compounds at levels compatible with cell growth or survival,

wherein if said cells have undergone LOH of said gene, then said patient is a potential patient for said treatment.

20

86. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the steps of:

25

identifying a patient heterozygous for a said gene encoding a product required to maintain cellular proteins at levels compatible with cell growth or survival;

wherein if said patient is heterozygous for said gene, then said patient is a potential patient for said treatment.

87. The method of claim 86, further comprising the step of determining whether cancer cells in said patient contain only a single allele of said gene,

wherein if said cancer cells contain only a single allele of said gene, then said patient is a potential patient for said treatment.

5

88. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the step of:

10

determining whether cancer cells in said patient have undergone LOH of a said gene encoding a product required to maintain cellular proteins at levels compatible with cell growth or survival,

wherein if said cells have undergone LOH of said gene, then said patient is a potential patient for said treatment.

15

89. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the steps of:

20

identifying a patient heterozygous for a said gene encoding a product required to maintain cellular nucleotides at levels compatible with cell growth or survival;

wherein if said patient is heterozygous for said gene, then said patient is a potential patient for said treatment.

25

90. The method of claim 89, further comprising the step of determining whether cancer cells in said patient contain only a single allele of said gene,

wherein if said cancer cells contain only a single allele of said gene, then said patient is a potential patient for said treatment.

91. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the step of:

5

determining whether cancer cells in said patient have undergone LOH of a said gene encoding a product required to maintain cellular nucleotides at levels compatible with cell growth or survival,

wherein if said cells have undergone LOH of said gene, then said patient is a potential patient for said treatment.

10

92. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the steps of:

15

identifying a patient heterozygous for a said gene encoding a product required to maintain the integrity and function of cellular and subcellular structures;

wherein if said patient is heterozygous for said gene, then said patient is a potential patient for said treatment.

20

93. The method of claim 91, further comprising the step of determining whether cancer cells in said patient contain only a single allele of said gene,

wherein if said cancer cells contain only a single allele of said gene, then said patient is a potential patient for said treatment.

25

94. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the step of:

determining whether cancer cells in said patient have undergone LOH of a

said gene encoding a product required to maintain the integrity and function of cellular and subcellular structures,

wherein if said cells have undergone LOH of said gene, then said patient is a potential patient for said treatment.

5

95. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the steps of:

10

identifying a patient heterozygous for a said gene located on a high frequency LOH chromosomal arm region;

wherein if said patient is heterozygous for said gene, then said patient is a potential patient for said treatment.

15

96. The method of claim 95, further comprising the step of determining whether cancer cells in said patient contain only a single allele of said gene,

wherein if said cancer cells contain only a single allele of said gene, then said patient is a potential patient for said treatment.

20

97. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the step of:

25

determining whether cancer cells in said patient have undergone LOH of a said gene located on a high frequency LOH chromosomal arm region,

wherein if said cells have undergone LOH of said gene, then said patient is a potential patient for said treatment.

98. A method of identifying a potential patient for treatment with an inhibitor

10

15

20

25

active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the steps of:

identifying a patient heterozygous for a said gene which has at least two sequence variances which occur at frequences such that at least 10% of a population is heterozygous for said gene;

wherein if said patient is heterozygous for said gene, then said patient is a potential patient for said treatment.

99. The method of claim 98, further comprising the step of determining whether cancer cells in said patient contain only a single allele of said gene,

wherein if said cancer cells contain only a single allele of said gene, then said patient is a potential patient for said treatment.

100. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a gene vital for cell growth or viability, wherein said patient is suffering from a cancer, said method comprising the step of:

determining whether cancer cells in said patient have undergone LOH of a said gene which has at least two sequence variances which occur at frequences such that at least 10% of a population is heterozygous for said gene,

wherein if said cells have undergone LOH of said gene, then said patient is a potential patient for said treatment.

101. A nucleic acid probe at least 12 nucleotides in length which is perfectly complementary to a portion of a first allelic form of a gene vital for cell growth or viability,

wherein said gene encodes a product required for cell proliferation, wherein said portion comprises a sequence variance site, and wherein said probe

WO 98/41648

232/116

hybridizes under stringent hybridization conditions to said portion and not to a corresponding portion of a second allelic form having at least one different nucleotide at said sequence variance site.

5

102. A nucleic acid probe at least 12 nucleotides in length which is perfectly complementary to a portion of a first allelic form of a gene vital for cell growth or viability,

10

wherein said gene encodes a product required to maintain inorganic ions and vitamins at levels compatible with cell growth or survival, wherein said portion comprises a sequence variance site, and wherein said probe hybridizes under stringent hybridization conditions to said portion and not to a corresponding portion of a second allelic form having at least one different nucleotide at said sequence variance site.

15

103. A nucleic acid probe at least 12 nucleotides in length which is perfectly complementary to a portion of a first allelic form of a gene vital for cell growth or viability,

20

wherein said gene encodes a product required to maintain organic compounds at levels compatible with cell growth or survival, wherein said portion comprises a sequence variance site, and wherein said probe hybridizes under stringent hybridization conditions to said portion and not to a corresponding portion of a second allelic form having at least one different nucleotide at said sequence variance site.

25

104. A nucleic acid probe at least 12 nucleotides in length which is perfectly complementary to a portion of a first allelic form of a gene vital for cell growth or viability,

wherein said gene encodes a product required to maintain cellular

proteins at levels compatible with cell growth or survival, wherein said portion comprises a sequence variance site, and wherein said probe hybridizes under stringent hybridization conditions to said portion and not to a corresponding portion of a second allelic form having at least one different nucleotide at said sequence variance site.

5

105. A nucleic acid probe at least 12 nucleotides in length which is perfectly complementary to a portion of a first allelic form of a gene vital for cell growth or viability,

10

wherein said gene encodes a product required to maintain cellular nucleotides at levels compatible with cell growth or survival, wherein said portion comprises a sequence variance site, and wherein said probe hybridizes under stringent hybridization conditions to said portion and not to a corresponding portion of a second allelic form having at least one different nucleotide at said sequence variance site.

15

106. A nucleic acid probe at least 12 nucleotides in length which is perfectly complementary to a portion of a first allelic form of a gene vital for cell growth or viability,

20

wherein said gene encodes a product required to maintain the integrity and function of cellular and subcellular structures, wherein said portion comprises a sequence variance site, and wherein said probe hybridizes under stringent hybridization conditions to said portion and not to a corresponding portion of a second allelic form having at least one different nucleotide at said sequence variance site.

25

107. A nucleic acid probe at least 12 nucleotides in length which is perfectly complementary to a portion of a first allelic form of a gene vital for cell growth or

WO 98/41648

PCT/US98/05419

viability,

5

10

15

20

25

wherein said gene is located on a high frequency LOH chromosomal arm region, wherein said portion comprises a sequence variance site, and wherein said probe hybridizes under stringent hybridization conditions to said portion and not to a corresponding portion of a second allelic form having at least one different nucleotide at said sequence variance site.

108. A nucleic acid probe at least 12 nucleotides in length which is perfectly complementary to a portion of a first allelic form of a gene vital for cell growth or viability,

wherein said gene has at least two sequence variances which occur at frequences such that at least 10% of a population is heterozygous for said gene, wherein said portion comprises a sequence variance site, and wherein said probe hybridizes under stringent hybridization conditions to said portion and not to a corresponding portion of a second allelic form having at least one different nucleotide at said sequence variance site.

109. The method ,inhibitor, pharmaceutical composition, or nucleic acid probe of any of claims 1, 13, 21, 29, 37, 53, 69, 77, and 101, wherein said gene is selected from the group consisting of 14-3-3 Protein TAU, CCNA(G2/Mitotic-Specific Cyclin A), CCNB1(G2/Mitotic-Specific Cyclin B1), CCND1(G1/S-Specific Cyclin D1), CCND2(G1/S-Specific Cyclin D2), CCND3(G1/S-Specific Cyclin D3), Cell division control protein 16, Cell division cycle 2, G1 to S and G2 to M, Cell division cycle 25A, Cell division cycle 25B, Cell division cycle 25C, Cell division cycle 27, Cell division-associated protein BIMB, Cyclin A1(G2/Mitotic-Specific Cyclin A1), Cyclin C (G1/S-Specific Cyclin C), Cyclin G1(G2/Mitotic-Specific Cyclin G), Cyclin G2 (G2/Mitotic-Specific Cyclin G), Cyclin H, Cyclin H Assembly, GSPT1(G1 to S phase transition 1), Mitotic MAD2 Protein, MRNP7, RANBP1(RAN binding protein 1), WEE1, Cell Division Protein Kinase 4, CDC28 protein kinase 1, CDC28 protein

WO 98/41648 PCT/US98/05419

369 232/116

kinase 2, M-Phase inducer phosphatase 2, M-phase phosphoprotein, mpp6, PPP1ca(Protein phosphatase 1, catalytic subunit, alpha isoform), STM7-LSB, CENP-F kinetochore protein, Centromere autoantigen C, Centromere protein B (80kD), Centromere protein E (312kD), CHC1(Chromosome condensation 1), Chromatin assembly factor-I p150 subunit, Chromatin assembly factor-I p60 subunit, Chromosome segregation gene homolog CAS, HMG1(High-mobility group (nonhistone chromosomal) protein 1), Minichromosome Maintenance (MCM7), Mitotic centromere-associated kinesin, RMSA1(Regulator of mitotic spindle assembly 1), and SUPT5h(Chromatin structural protein homolog (SUPT5H)).

10

15

20

25

5

The method ,inhibitor, pharmaceutical composition, or nucleic acid probe of any of claims 2, 14, 22, 30, 39, 55, 70, 80, and 102, wherein said gene is selected from the group consisting of PMCA1 (Calcium Pump), PMCA2 (Calcium Pump), PMCA3 (Calcium Pump), PMCA4 (Calcium Pump), ATP2b1 (Calcium-Transporting ATPase Plasma Membrane), ATP2b2 (Calcium-Transporting ATPase Plasma Membrane), ATP2b4 (Calcium-Transporting ATPase Plasma Membrane), ATP5b (ATP Synthase Beta Chain, Mitochondrial Precursor), Chloride Conductance Regulatory Protein ICLN, H-Erg (Potassium Channel Protein EAG), Nuclear Chloride Ion Channel Protein (NCC27), SCN1b(Sodium Channel, Voltage-Gated, Type I, Beta Polypeptide), Two P-Domain K+ Channel TWIK-1, VDAC2 (Voltage-Dependent Anion-Selective Channel Protein 2), ATP1b1 (Sodium/Potassium-Transporting ATPase Beta-1 Chain), ATP1b2 (Sodium/Potassium-Transporting ATPase Beta-2 Chain), ATPase, Ca++ transporting, plasma membrane 4, ATPase, Ca++ transporting, plasma membrane 2, ATPase, Na+/K+ transporting, alpha 1 polypeptide, ATPase, Na+/K+ transporting, alpha 3 polypeptide, ATPase, Na+/K+ transporting, beta 1 polypeptide, ATPase, Na+/K+ transporting, beta 2 polypeptide. Na+.K+ ATPase, 1 Subunit, Na+,K+ ATPase, 2 alpha, Na+,K+ ATPase, 3 beta, SLC9a1(Solute carrier family 9 (sodium/hydrogen exchanger)), Solute carrier family 4, anion exchanger, member 1, Solute carrier family 4, anion

WO 98/41648

PCT/US98/05419

exchanger, member 2, Solute carrier family 9 (sodium/hydrogen exchanger), Passive transporters, Maxik Potassium Channel Beta Subunit, Chloride Channel 2, Chloride Channel Protein (CLCN7), TRPC1 (Transient Receptor Potential Channel 1), Potassium Channel Kv2.1, ATP5d(ATP synthase, H+ transporting, mitochondrial F1 complex, delta subunit), ATP5f1(ATP synthase, H+ transporting, mitochondrial F0 complex, subunit b), ATP50(ATP synthase, H+ transporting, mitochondrial F1 complex. O subunit). ETFa(Electron-transfer-flavoprotein, alpha polypeptide (glutaric aciduria II)). ETFb(Electron-transfer-flavoprotein, beta polypeptide), Nadhubiquinone oxidoreductase 13 kd-B subunit, Nadh-ubiquinone oxidoreductase 39 kD subunit precursor, NADH-Ubiquinone oxidoreductase 75 kD subunit precursor, NADH-Ubiquinone oxidoreductase **MFWE** subunit, NDUFV2(NADH dehydrogenase (ubiquinone) flavoprotein 2 (24kD)), Ubiquinol-cytochrome c reductase complex 11 kD, ATP Synthase Alpha Chain, NADH dehydrogenaseubiquinone Fe-S protein 8, 23 kDa subunit, Ascorbic Acid (transporter), Folate Binding Protein, Folate receptor 1 (adult), Nicotinamide (transporter), Pantothenic Acid transporter, Riboflavin (transporter), SCL19A1 (Solute Carrier Family 19, Member 1), Solute carrier family 19 (folate transporter), member 1, Thiamine, B6, B12 (transporter), ATP7b (Copper-Transporting ATPase 2), Ceruloplasmin (ferroxidase), Ceruloplasmin receptor (Copper Transporter), Copper Transport Protein HAH1, Molybdenum, Selenium, Tranferrin Receptor (Iron Transporter), Zinc Transporter, and mitochondrial import receptor subunit TOM20.

25

5

10

15

20

111. The method ,inhibitor, pharmaceutical composition, or nucleic acid probe of 3, 25, 23, 31, 41, 57, 71, 83, and 103, wherein said gene is selected from the group consisting of GLUT1, GLUT2, GLUT3, GLUT4, GLUT5, GLUT6, Solute carrier family 5 (sodium/glucose cotransporter), Solute carrier family 2 (facilitated glucose transporter), member 2, Solute carrier family 2 (facilitated glucose transporter) member 5, Solute carrier family 3 member 1, System b,(Na+ independent), System y,(Na+ independent), ATRC1(Catioinc), LEUT(Leucine Transporter),

232/116

SLC1A1(Solute Carrier Family 1, Member 1), Solute carrier family 16 (monocarboxylic acid transporters), ACO1(Aconitase 1), ACO2(Aconitase 2, mitochondrial), Acyl-Coenzyme A dehydrogenase, C-2 to C-3 short chain, Acyl-Coenzyme A dehydrogenase, C-4 to C-12 straight chain, Acyl-Coenzyme A dehydrogenase, long chain, Acyl-Coenzyme A dehydrogenase, very long chain, aKGD (alpha ketoglutaratedehydrogenase), ALD-a (Aldolase), ALD-b (Aldolase), ALD-c (Aldolase), CS (Citrate Synthetase), Dihydrolipoamide S-succinyltransferase, DLAT(Dihydrolipoamide S-acetyltransferase (E2 component of pyruvate dehydrogenase complex)), DLD(Dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)), E1k (Oxoglutarate dehydrogenase). E2k (Dihydrolipoamide S-succinyltransferase), E3 (Dihydrolipoyl Dehydrogenase), ENO1(Enolase 1,alpha), ENO2(Enolase 2), ENO3(Enolase 3), Enolase 2, (gamma, neuronal), Enolase 3, (beta, muscle), FH(Fumarate hydratase), G3PDH (Glyceraldehyde-3-Phosphate Dehydrogenase), G6PD (Glucose-6-Phosphate Dehydrogenase), Glucose-6-phosphate dehydrogenase, HK1 (Hexokinase 1), HK2 (Hexokinase 2), HK3 (Hexokinase 3), IDH1(Isocitrate dehydrogenase 1 (NADP+). soluble). IDH2(Isocitrate dehydrogenase 2 (NADP+), mitochondrial), MDH1(Malate dehydrogenase 1, NAD (soluble)), MDH2(Malate dehydrogenase 1, NAD (mitochondrial)), NAD(H)-specific isocitrate dehydrogenase alpha subunit, Oxoglutarate dehydrogenase (lipoamide), PDHB (Pyruvate Dehydrogenase), PDHB(Pyruvate dehydrogenase (lipoamide) beta), PDK4 (Pyruvate dehydrogenase kinase, isoenzyme 4), PFKL(Phosphofructokinase), PGI (Phosphoglucoisomerase), PGKa (Phosphoglyceromutase), **PGKb** (Phosphoglyceromutase), PGM1 (Phosphoglyceromutase), PGM2 (Phosphoglyceromutase), PGM3 (Phosphoglyceromutase), PGM4 (Phosphoglyceromutase), Phosphofructokinase, muscle, Phosphoglucomutase 1, Phosphoglycerate kinase 1, PK1 (Pyruvate Kinase), PK2 (Pyruvate Kinase), PK3 (Pyruvate Kinase), Pyruvate dehydrogenase kinase isoenzyme 2 (PDK2), Pyruvate kinase, liver, Pyruvate kinase, muscle,

25

5

10

15

232/116

SDH1(Succinate dehydrogenase, iron sulphur (Ip) subunit), SDH2(Succinate dehydrogenase 2, flavoprotein (Fp) subunit), TKT(Transketolase (Wernicke-Korsakoff syndrome)), TPI (Trisephosphate Isomerase), Asparagine Synthetase, Aminoacylase-1, Aminoacylase-2, ACAC (Acetyl CoA Carboxylase Beta), ACAC (Acetyl CoA Carboxylase), ACADSB(Acyl-coA dehydrogenase), Mevalonate kinase, Phosphomevalonate kinase, Aspartoacylase, Ornithine decarboxylase 1, Short-acyl-CoA dehydrogenase, Medium acyl-CoA dehydrogenase, Long acyl-CoA dehydrogenase, Isovalveryl CoA dehydrogenase, 2-methyl branched chain, Adenosine Deaminase, Purine-nucleoside phosphorylase, Guanine Deaminase, Xanthine Oxidase, ITM1 (Integral Transmembrane Protein), GFPT (Glutamine-Fructose-6-Phosphate Transaminase), Heparan, Polypeptide N-Acetyltransferase, ACAA(Acetyl-Coenzyme A acyltransferase), Lysophosphatidic acid acyltransferasealpha, Lysophosphatidic acid acyltransferase-beta, FNTa (Farnesyltransferase Alpha Subunit), FNTb (Farnesyltransferase Beta Subunit), NMT1 (N-myristoyltransferase), Calcineurin A, Calcineurin B, Calreticulin Precursor, Phosphatase 2b. PPP3ca(Protein phosphatase 3, catalytic subunit), SNK Interacting 2-28(Calcineurin B Subunit), Protein Kinase C, PRKCA(Protein kinase C, alpha), PRKCB1(Protein kinase C, beta 1), PRKCD(Protein kinase C, delta), PRKCM(Protein kinase C, mu), PRKCQ(Protein kinase C-theta), PRKCSH(Protein kinase C substrate 80K-H), Geranylgeranyl, Geranylgeranyltransferase (Type I Beta), **GGTB** (Geranylgeranyltransferase), Geranylgeranyltransferase (Type II Beta-Subunit), Gdp Dissociation Inhibitors, GDI Alpha (RAB GDP Dissociation Inhibitor Alpha), and Rab Gdp (RAB GDP Dissociation Inhibitor Alpha).

25

5

10

15

20

112. The method, inhibitor, pharmaceutical composition, or nucleic acid probe of any of claims 4, 16, 24, 32, 43, 59, 72, 86, and 104, wherein said gene is selected from the group consisting of GOT(Glutamic-oxaloacetic transaminase 2), GOT1(Glutamic-oxaloacetic transaminase 1), PYCS(Pyrroline-5-carboxylate synthetase), Tyrosine aminotransferase, AARS, CARS, DARS, EPRS, FARS,

GARS, HARS, IARS, KARS, LARS, MARS, NARS, QARS, RARS, SARS, TARS, VARS, WRS, YARS, Ribosomal Protein L11, Ribosomal Protein L12, Ribosomal Protein L17, Ribosomal Protein L18, Ribosomal Protein L18a, Ribosomal Protein L19, Ribosomal Protein L21, Ribosomal Protein L22, Ribosomal Protein L23, Ribosomal Protein L23a, Ribosomal Protein L25, Ribosomal Protein L26, Ribosomal Protein L27, Ribosomal Protein L27a, Ribosomal Protein L28, Ribosomal Protein L29, Ribosomal Protein L30, Ribosomal Protein L31, Ribosomal Protein L32, Ribosomal Protein L35, Ribosomal Protein L35a, Ribosomal Protein L36a, Ribosomal Protein L39, Ribosomal Protein L4, Ribosomal Protein L41, Ribosomal Protein L44, Ribosomal Protein L6, Ribosomal Protein L7, Ribosomal Protein L7a, Ribosomal Protein L8, Ribosomal Protein L9, Ribosomal Protein P1, Ribosomal Protein S10, Ribosomal Protein S11, Ribosomal Protein S13, Ribosomal Protein S14, Ribosomal Protein S15, Ribosomal Protein S15A, Ribosomal Protein S16, Ribosomal Protein S17, Ribosomal Protein S17A, Ribosomal Protein S17B, Ribosomal Protein S18, Ribosomal Protein S20, Ribosomal Protein S20A, Ribosomal Protein S20B, Ribosomal Protein S21, Ribosomal Protein S23, Ribosomal Protein S25, Ribosomal Protein S26, Ribosomal Protein S28, Ribosomal Protein S29, Ribosomal Protein S3, Ribosomal Protein S3A, Ribosomal Protein S4, Ribosomal Protein S4X, Ribosomal Protein S4Y, Ribosomal Protein S5, Ribosomal Protein S6, Ribosomal Protein S7, Ribosomal Protein S8, Ribosomal Protein S9, Initiation of polypeptide polymerization, eIF-2 (Eukaryotic initiation factor), eIF-2associated p67(Eukaryotic initiation factor), eIF-2A(Eukaryotic initiation factor), eIF-2Alpha(Eukaryotic initiation factor), eIF-2B(Eukaryotic initiation factor), eIF-2B-Gamma(Eukaryotic initiation factor), eIF-2Beta(Eukaryotic initiation factor), eIF-3 p110(Eukaryotic initiation factor), eIF-3 p36(Eukaryotic initiation factor), eIF-4A(Eukaryotic initiation factor), eIF-4C(Eukaryotic initiation factor), eIF-4E(Eukaryotic initiation factor), eIF-4Gamma(Eukaryotic initiation factor), eIF-5(Eukaryotic initiation factor), eIF-5A, Eukaryotic peptide chain release factor subunit 1, P97(Eukaryotic initiation factor), eEF1A2(Eukaryotic elongation factor),

20

15

5

10

10

15

20

25

eEF1D(Eukaryotic elongation factor), eEF2(Eukaryotic elongation factor), eIF4A2 (Eukaryotic initiation factor), KIAA0031(Elongation factor 2), KIAA0219(Putative translational activator C18G6.05C), Factor 1-Alpha 2(Eukaryotic translation elongation factor 1 alpha 2), Cis-Trans Isomerase, DNAj Protein Homolog 1, DNAj Protein Homolog 2, DNAJ Protein homolog HSJ1, T-Complex. Aspartylglucosaminidase, T-Complex 1, Alpha, T-Complex 1, Epsilon, T-Complex 1, Gamma, T-Complex 1, Theta, T-Complex 1, Zeta, 26S Protease regulatory subunit 4, Alpha-2-Macroglobulin, Calpain 1, Large, CLPP(ATP-Dependent CLP protease proteolytic subunit), KIAA0123 (Mitochondrial processing peptidase alpha subunit), MMP7, Proteasome Beta 6, Proteasome Beta 7, Proteasome C13, Proteasome C2, Proteasome C7-1, Proteasome inhibitor hPI31 subunit, Proteasome P112, Proteasome P27, Proteasome P55, Enzyme E2-17 Kd(Cyclin-selective ubiquitin carrier protein), ISOT-3(Ubiquitin carboxyl-terminal hydrolase T), ORF (Ubiquitin carboxyl-terminal hydrolase 14), PGP(Ubiquitin carboxyl-terminal hydrolase isozyme L1), UBA52(Ubiquitin A-52 residue ribosomal protein fusion product 1), Ubiquitin carboxyl-terminal hydrolase 3, Ubiquitin carboxyl-terminal hydrolase isozyme L3, Ubiquitin carboxyl-terminal hydrolase T, Ubiquitin carrier protein (E2-EPF), Ubiquitin fusion-degradation protein (UFD1L), Ubiquitin Hydrolase, Ubiquitin-conjugating enzyme E2I, SEC23(Protein transport protein SEC23), SEC23A(Protein transport protein SEC23), SEC7(Protein transport protein SEC7), SEC61 (Beta Subunit), and LDLR (LDL receptor).

113. The method, inhibitor, pharmaceutical composition, or nucleic acid probe of any of claims 5, 17, 25, 33, 45, 73, 89, and 105, wherein said gene is selected from the group consisting of Adenylate Kinase-2, Adenylosuccinate synthetase, Adenylosuccinate Lyase, DPRT (ADP-Ribosyltransferase), ADSL (Adenylosuccinate lyase/AMP synthetase), ADSS (Adenylosuccinate Synthetase), CAD PROTEIN, CTP Synthetase, CTPS(CTP synthetase), Cytidine Triphosphate Synthetase, GARS (Phosphoribosylglycinamide synthetase), GART (Phosphoribosylglycinamide

10

15

20

25

formyltransferase). GART(Phosphoribosylglycinamide formyltransferase, phosphoribosylglycinamide synthetase, phosphoribosylaminoimidazole synthetase), GMP Synthetase, IMP Cyclohydrolase, IMP dehydrogenase, IMPDH1(IMP (inosine monophosphate) dehydrogenase 1), IMPDH2(IMP (inosine monophosphate) dehydrogenase 2), Phosphoribosyl diphosphotransferase. Phosphoribosylaminoimidazolecarboxamide formyltransferase, Phosphoribosylformylglycinamide synthetase, Phosphoribosylglycinamide carboxylase, Phosphoribosylglycinamide-succinocarboxamide synthetase, PPAT (Amidophoribosyltransferase), PPAT(Phosphoribosyl pyrophosphate amidotransferase), Ribonucleoside-diphosphate reductase M1 chain, Ribonucleosidediphosphate reductase M2 chain, Thymidine Kinase, Thymidylate Synthase, UMK(Uridine kinase), UMPK (Uridine monophosphate kinase), UMPS(Uridine monophosphate synthetase (orotate phosphoribosyl transferase and orotidine-5'decarboxylase)), Uridine Phosphorylase, DNA Origin Recognition Complex, ORC1, ORC2, ORC3, ORC4, ORC5, ORC6, ORC Regulators, CDC6, CDC7, CDC1, DNA Polymerization, DNA Polymerases, Adprt (NAD(+)Ribosyltransferase), DNA Polymerase Alpha-Subunit, DNA Polymerase Delta, POLa(DNA Polymerase Alpha/Primase Associated Subunit), POLb(DNA Polymerase Beta Subunit), POLd1(Polymerase (DNA directed), Delta 1, Catalytic Subunit), POLd2(Polymerase (DNA directed), Delta 2), POLE(Polymerase (DNA directed)), POLg (DNA Polymerase Gamma Subunit), Terminal Transferase (DNA Nucleotidylexotransferase), Activator 1 36 Kd, CDC46 (DNA Replication Licensing Factor), CDC47 (DNA Replication Licensing Factor CDC47), DNA Topoisomerase III, DRAP1 (DNA Replication Licensing Factor MCM3), KIAA0030 Gene (Cell Division Control Protein 19), KIAA0083 Gene (DNA Replication Helicase DNA2), MCM3 (DNA Replication Licensing Factor MCM3), PCNA (Proliferating Cell Nuclear Antigen), PRIM1 (DNA Primase 49 kD Subunit), PRIM2 (DNA Primase), PRIM2a (DNA Primase 58 kD Subunit), PRIM2b (DNA Primase), RECa (Replication Protein A 14 kD Subunit), RFC1 (Replication Factor C (activator 1) 1),

RFC2 (Replication Factor C 2), RFC3 (Replication Factor C (activator 1) 3), RFC4 (Replication Factor C, 37-kD subunit), RFC5 (Replication Factor C), RPA1 (Replication protein A1 (70kD)), RPA2 (Replication protein A2 (32kD)), RPA3 (Replication protein A3 (14kD)), TOP1 (DNA Topoisomerase I), TOP2a (Topoisomerase (DNA) II Alpha (170kD)), TOP2b (Topoisomerase (DNA) II Beta (180kD)), CHL1(CHL1-Related Helicase), DNA Helicase II, Mi-2(Chromodomain-Helicase- DNA-Binding Protein CHD-1), RECOL (ATP-Dependent DNA Helicase Q1), Smbp2 (DNA-Binding Protein SMUBP-2), H1(0) (Histone H5A), Histone H1d. Histone H1x, Histone H2a.1, Histone H2a.2, Histone H2b.1, Histone H4, SLBP (Histone Hairpin-Binding Protein), TATA-binding Complex, Small Nuclear RNA-Activating Complex, Polypeptide 1, 43KD (SNAPC1), Small Nuclear RNA-Activating Complex, Polypeptide 2, (SNAPC2), Small Nuclear RNA Activating Complex, Polypeptide 3, 50KD (SNAPC3), TAF2D(TBP-associated factor), TAFII100(TBP-associated factor), TAFII130(TBP-associated factor), TAFII20(TBPassociated factor), TAFII250(TBP-associated factor), TAFII28(TBP-associated factor), TAFII30(TBP-associated factor), TAFII32(TBP-associated factor), TAFII40(TBP-associated factor), TAFII55(TBP-associated factor), TAFII80(TBPassociated factor), TBP(TATA Binding Protein), TMF1 (TATA Element Modulatory Factor 1), RPB 7.0, RPB 7.6, RPB 17, RPB 14.4, RNA polymerase I subunit hRPA39, 13.6 Kd Polypeptide (DNA-Directed RNA Polymerase II 13.6 kD Polypeptide), POLR2C(RNA polymerase II, polypeptide C (33kD)), Polypeptide A (220kd), RNA Polymerase II 23k, RNA polymerase II holoenzyme component (SRB7), RNA polymerase II subunit (hsRPB10), RNA polymerase II subunit (hsRPB8), RNA polymerase II subunit hsRPB4, RNA polymerase II subunit hsRPB7, RNA Polymerase II Subunit(DNA- Directed RNA Polymerases I, II, and III 7.3 kD polypeptide), TCEB1L(Transcription elongation factor B (SIII), polypeptide 1-like), RNA polymerase III subunit (RPC39), RNA polymerase III subunit (RPC62), Elongation Factor 1-Beta, Elongation Factor S-II, TCEA (110kD), TCEB1, TCEB (18kD), TCEB1L, TCEB3, TCEC (15kDa), TFIIS (Transcription

10

5

15

20

PCT/US98/05419

377 232/116

Elongation Factor IIS), E2F1 (E2F Transcription Factor), TFAP2A (Transcription Factor A2 Alpha), TFCP2 (Transcription Factor CP2), TFC12 (Transcription Factor 12), PRKDC (Protein Kinase, DNA activated catalytic subunit), SUPT6H, TFIIA gamma subunit, TFIIA delta, TFIIB related factor hBRF (HBRF), TFIIE Alpha Subunit, TFIIE Beta Subunit, TFIIF, Beta Subunit, GTF2F1 (TFIIF), GTF2F2 (TFIIF), General Transcription Factor IIIA, TFIIH(52 kD subunit of transcription factor), TFIIH(p89), TFIIH(p80), TFIIH(p62), TFIIH(p44), TFIIH(p34), Transcription Factor IIf(General transcription factor IIF, polypeptide 1 (74kD subunit))Transcription Factor IIf(General transcription factor IIF, polypeptide 1 (74kD subunit)), BTF 62 kDSubunit (Basic transcription factor 62 kD subunit), CAMP-dependent transcription factor ATF-4, CCAAT box-binding transcription factor 1, CRM1(Negative regulator CRM1), Cyclic-AMP-dependent transcription factor ATF-1, GABPA(GA-binding protein transcription factor, alpha subunit (60kD)), ISGF-3(Signal transducer and activator of transcription 1-alpha/beta), NFIX(Nuclear factor I/X (CCAAT-binding transcription factor)), NFYA(Nuclear transcription factor Y, alpha), NTF97(Nuclear factor p97), Nuclear factor I-B2 (NFIB2), Nuclear factor NF45, Nuclear factor NF90, POU2F1(POU domain, class 2, transcription factor 1), Sp2 transcription factor, TCF12(Transcription factor 12 (HTF4, helix-loop-helix transcription factors 4)), TCF3(Transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47)), TCF6L1(Transcription factor 6-like 1), TF P65(Transcription factor p65), TFCOUP2(Transcription factor COUP 2 (a.k.a. ARP1)), Transcription factor IL-4 Stat, Transcription Factor S-II (Transcription factor S-II-related protein), Transcription factor Stat5b, Transcription Factor, Transcription factor (CBFB), 9G8 Splicing Factor (Pre-mRNA Splicing SRP20), CC1.3(Splicing factor (CC1.3)), HnRNP F protein, A2/B1), HNRPA2B1(Heterogeneous nuclear ribonucleoproteins HNRPG(Heterogeneous nuclear ribonucleoprotein G), HNRPK(Heterogeneous nuclear ribonucleoprotein K). Pre-mRNA splicing factor helicase, Pre-mRNA splicing factor SF2, P33 subunit, Pre-mRNA splicing factor SRP20, Pre-mRNA

5

10

15

20

10

15

20

25

114.

splicing factor SRP75, PRP4(Serine/threonine-protein kinase PRP4), PTB-Associated Splicing Factor, Ribonucleoprotein A', Ribonucleoprotein A1, Ribonucleoprotein C1/C2, RNP Protein, L (Heterogeneous nuclear ribonucleoprotein L), RNP-Specific C(U1 small nuclear ribonucleoprotein C), SAP 145(Spliceosome associated protein), SAP 61(Splicesomal protein), SC35(Splicing factor), SF3a120, SFRS2(Splicing factor, arginine/serine-rich 2), SFRS5(Splicing factor, arginine/serine-rich 5), SFRS7(Splicing factor, arginine/serine-rich 7), Small nuclear ribonucleoprotein SM D1, SnRNP core protein Sm D2, SnRNP core protein Sm D3, SNRP70(U1 snRNP 70K protein), SNRPB(Small nuclear ribonucleoprotein polypeptides B and B1), SNRPE(Small nuclear ribonucleoprotein polypeptide E), SNRPN(Small nuclear ribonucleoprotein polypeptide N), Splicing factor SF3a120, Splicing factor U2AF 35 kD subunit, Splicing factor U2AF 65 kD subunit, SRP30C(Pre-mRNA splicing factor SF2, p33 subunit), SRP55-2(Pre-mRNA splicing factor SRP75), Transcription factor BTEB, Transcription initiation factor TFIID 250 kD subunit, Cleavage and polyadenylation specificity factor, Cleavage stimulation factor, 3' pre-RNA, subunit 1, 50kD, Cleavage stimulation factor, 3' pre-RNA, subunit 3, 77kD, HNRNP Methyltransferase, PABPL1(Poly(A)-binding protein-like 1), Pap mRNA(Poly(A) Polymerase), RNA unwinding, RNA Helicase, GU Protein (ATP-Dependent RNA helicase dead), KIAA0224 Gene(Putative ATP-dependent RNA helicase), RNA Helicase A, RNA Helicase P110, and Ste13(Nuclear RNA Helicase).

any of claims 6, 18, 26, 34, 47, 63, 92, and 106, wherein said gene is selected from the group consisting of AP47(Clathrin Coat Assembly AP47), AP50(Clathrin Coat Assembly Protein AP50), Cell Surface Protein (Clathrin Heavy Polypeptide-Like Protein), Cltb(Clathrin Light Chain B), Cltc (Clathrin Heavy Chain), Adenylate Cyclase, Adenylate Cyclase, Adenylate Cyclase, II, Adenylate Cyclase, IV, Complex I, MTND1 (Subunit ND1), MTND2 (Subunit ND2), MTND3 (Subunit ND3),

MTND4 (Subunit ND4), MTND4L (Subunit ND4L), MTND5 (Subunit ND5),

The method, inhibitor, pharmaceutical composition, or nucleic acid probe of

5

10

15

20

25

MTND6 (Subunit ND6), Complex II, Complex III, Cytochrome b subunit, Complex IV, CO1 (Cytochrome c Oxidase Subunit I), CO2 (Cytochrome c Oxidase Subunit 2), CO3 (Cytochrome c Oxidase Subunit 3), Complex V, ATP Synthase Subunit ATPase 6, Kinesin Heavy Chain, Kinesin Light Chain, Syntaxin 1a, Syntaxin 1b, Syntaxin 3, Syntaxin 5a, Syntaxin 7, CANX (Calnexin), ER Lumen Protein 1, ER Lumen Protein 2, Ribophorin I, Ribophorin II, Signal recognition particle receptor. SRP Protein, TIM17 preprotein translocase, Golgin-245, TGN46 (Trans-Golgi Network Integral Membrane Protein TGN38 Precursor), Beta-Cop, Coatomer Beta' Subunit, Coatomer Delta Subunit, Gp36b Glycoprotein (Vesicular integral-membrane protein VIP36 precursor), Homologue of yeast sec7, Protein transport protein SEC13 (Chromosome 3p25), SEC14 (S. Cerevisiae), Synaptic vesicle membrane protein VAT-1, Synaptobrevin-3, Synaptotagmin I, Transmembrane(COP-coated vesicle membrane protein p24 precursor), Vacuolar-Type (Clathrin-coated vesicle/synaptic vesicle proton pump 116 kd subunit), 140 kD Nucleolar phosphoprotein, Autoantigen p542, Export protein Rae1 (RAE1), Heterogeneous nuclear ribonucleoprotein A1, Nuclear pore complex protein hnup153, Nuclear pore complex protein NUP214, Nuclear pore glycoprotein p62, Nuclear Transport Factor 2, Nucleoporin 98 (NUP98), NUP88, Ribonucleoprotein A, Ribonucleoprotein B", Karyopherin, Importin Alpha Subunit, TRN (Transportin), Actin, Beta-Centractin, Capping Protein Alpha, CFL1 (Cofilin, Non-Muscle Isoform), Desmin, Dystrophin, Gelsolin, hOGG1(Myosin Light Chain Kinase), IC Heavy Chain, Itga2 (Integrin, Alpha 2 (CD49B, alpha 2 Subunit of VLA-2 receptor)), Itga3 (Integrin Alpha-3 Precursor), Keratin 19, Keratin, Type II, Lamin A, LBR(Lamin B Receptor), Light Chain Alkali, MacMarcks mRNA, MAP1a (Microtubule-Associated Protein 1A), MAP2(Microtubule-Associated Protein 2), MEG1(Protein-Tyrosine Phosphatase MEG1), Microtubule-Associated Protein TAU, Suppressor Of Tubulin STU2, TUBg (Tubulin Gamma Chain), Tubulin Alpha-4 Chain, USH1b (Myosin II Heavy Chain), Villin, Villin 2 (Ezrin), Actin Depolymerizing, Capping (Actin Filament), MYH9(Myosin, Heavy Polypeptide 9, Non-Muscle), MYL5(Myosin Regulatory Light Chain 2), Myosin Heavy Chain 95F, Myosin Heavy Chain IB, Myosin IB, Sh3p17(Myosin IC Heavy Chain), Sh3p18(Myosin IC Heavy Chain), KIAA0059(Dematin:Actin-Bundling Protein), TTN (Titin:Myosin Light Chain Kinase), ATP6c(Vacuolar H+ ATPase proton channel subunit), ATP6a1 (ATPase, H+ Transporting, Lysosomal (Vacuolar Proton Pump), Alpha Polypeptide, 70kD), ATP6b1(ATPase, H+ transporting, lysosomal (vacuolar proton pump), beta polypeptide, 56/58kD), ATP6d(ATPase, H+ transporting, lysosomal (vacuolar proton pump) 42kD), ATP6e(ATPase, H+ transporting, lysosomal (vacuolar proton pump) 31kD), ATPase, H+ transporting, lysosomal (vacuolar proton pump) 31kD, and Superoxide Dismutase.

10

5

115. A method for identifying an inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on a conditionally essential gene, and wherein said gene is subject to loss of heterozygosity in a cancer, said method comprising the steps of:

15

(a) determining at least two alleles of a said gene;

(b) testing a potential allele specific inhibitor to determine whether said potential allele specific inhibitor is active on at least one but less than all of said alleles;

wherein inhibition of expression of at least one but less than all of said alleles or reduction of the level of activity of a product of at least one but less than all of said alleles in the presence of said potential allele specific inhibitor is indicative that said potential allele specific inhibitor is a said inhibitor.

20

116. An inhibitor potentially useful for treatment of cancer, wherein said inhibitor is active on an allelic form of a conditionally essential gene, said gene has at least two alternative alleles in a population, and

25

wherein said inhibitor targets at least one but less than all of said alternative alleles.

117. A pharmaceutical composition, comprising

WO 98/41648 PCT/US98/05419

232/116

at least one allele specific inhibitor targeting at least one but less than all allelic forms of a conditionally essential gene in a population; and

a pharmaceutically acceptable carrier or excipient.

5

118. A method for producing an inhibitor potentially useful for cancer treatment, wherein said inhibitor is active on at least one but less than all alternative alleles of a conditionally essential gene having at least two alternative alleles, comprising the steps of:

10

- (a) identifying a conditionally essential gene that has alternative allelic forms in a noncancerous cell, wherein one of said alternative allelic forms is deleted in a cancer cell;
- (b) screening to identify an inhibitor which inhibits said at least one but less than all of said at least two alternative alleles; and
- (c) synthesizing said inhibitor in an amount sufficient to produce a therapeutic effect when administered to a patient suffering from a cancer in whom cancerous cells have only an allele of said gene inhibited by said inhibitor and in whom normal cells are heterozygous for said gene and contain an allelic form not inhibited by said inhibitor.

20

15

- 119. A method for preventing the development of cancer in a patient having a precancerous condition, comprising the steps of:
- a. subjecting cells of said precancerous condition to an altered condition such that a first conditionally essential becomes essential;

25

b. administering to said patient a therapeutic amount of a first allele specific inhibitor targeted to an allele of said first conditionally essential gene present in cells of said precancerous condition, wherein the normal somatic cells of said patient are heterozygous for said first gene, said inhibitor is active on at least one but less than all allelic forms of said gene present in a population and targets only one allelic form present in said normal somatic cells; and

5

10

15

20

25

wherein cells of said precancerous condition have undergone LOH of said first gene.

120. The method of claim 119, wherein the cells of said precancerous condition are not clonal from a single cell, further comprising the step of:

- c. serially administering to said patient at least one additional allele specific inhibitor, wherein each of said at least one additional allele specific inhibitors targets a different allele of a conditionally essential gene or an essential gene than is targeted by said first allele specific inhibitor, wherein said different allele may be a different allele of said first gene or an allele of a different gene, and wherein said patient is heterozygous for each targeted gene and each targeted gene has undergone LOH in cells of said precancerous condition.
- 121. A method for treating a patient suffering from a cancer, wherein said patient is heterozygous for a conditionally essential gene, comprising the steps of:
- a) subjecting cells of said cancer to altered conditions such that said gene is essential; and

administering a therapeutic amount of an allele specific inhibitor active on at least one but less than all allelic forms of said gene present in a population,

wherein said allele specific inhibitor inhibits only one allelic form of said gene present in said patient, and said only one allelic form of said gene is present in cancer cells in said patient.

- 122. The method of claim 121, further comprising the steps of:
- (a) determining whether non-cancerous cells of said patient are heterozygous for a particular conditionally essential gene; or
- (b) determining whether cancerous cells of said patient have only one allele of said particular gene; or
 - (c) both (a) and (b).

WO 98/41648

5

10

15

20

25

- 123. A method of inhibiting growth of a cell comprising the steps of:
 - a) subjecting said cell to conditions such that said gene is essential; and
- b) administering at least one inhibitor active on an allele of said conditionally essential gene,

wherein said inhibitor is less active on at least one other allele of said gene.

124. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a conditionally essential gene, wherein said patient is suffering from a cancer, said method comprising the step of:

identifying a patient heterozygous for a said gene,

wherein if said patient is heterozygous for said gene, then said patient is a potential patient for said treatment.

125. The method of claim 124, further comprising the step of determining whether cancer cells in said patient contain only a single allele of said gene,

wherein if said cancer cells contain only a single allele of said gene, then said patient is a potential patient for said treatment.

126. A method of identifying a potential patient for treatment with an inhibitor active on at least one but less than all alleles of a conditionally essential gene, wherein said patient is suffering from a cancer, said method comprising the step of:

determining whether cancer cells in said patient have undergone LOH of a said gene,

wherein if said cells have undergone LOH of said gene, then said patient is a potential patient for said treatment.

126. A nucleic acid probe at least 12 nucleotides in length which is perfectly complementary to a portion of a first allelic form of a conditionally essential gene, wherein said portion comprises a sequence variance site, and wherein

said probe hybridizes under stringent hybridization conditions to said portion and not to a corresponding portion of a second allelic form having at least one different nucleotide at said sequence variance site.

5

10

- 127. A method for selecting a patient for treatment with an antiproliferative treatment, comprising the steps of:
- a) determining whether normal somatic cells in a potential patient are heterozygous for an essential or conditionally essential gene, wherein a first allelic form of said gene is more active than a second allelic form, and wherein a reduction in the activity of said gene in a cell increases the sensitivity of said cell to a said antiproliferative treatment; and
- b) determining whether cancer cells of said patient have only said second allelic form of said gene,

wherein if said somatic cells are heterozygous and said cancer cells have only said second allelic form, it is indicative that said patient is suitable for treatment with said antiproliferative treatment.

15

128. A method for selecting an antiproliferative treatment for a patient suffering from a cancer, comprising the steps of:

20

a) determining whether normal somatic cells in a potential patient are heterozygous for an essential or conditionally essential gene which reduces the sensitivity of cells to an antiproliferative treatment, wherein a first allelic form of said gene is more active than a second allelic form, and wherein a reduction in the activity of said gene in a cell increases the sensitivity of said cell to a said antiproliferative treatment; and

25

b) determining whether cancer cells of said patient have only said second allelic form of said gene,

wherein if said somatic cells are heterozygous for said gene and said cancer cells have only said second allelic form, it is indicative that said antiproliferative treatment is suitable for said patient.

129. The method of any of claims 115-129, wherein said gene is selected from the group consisting of:

5

10

15

galactose-1-phosphate uridyltransferase, galactose kinase, UDP galactose-4epimerase, methionine synthase, asparagine synthase, glutamine synthetase, multidrug resistance gne/Pglycoprotein, multidrug resistance associated proteins 1-5, bleomycin hydrolase, dihydropyrimidine dehydrogenase, β-ureidopropoinase, β-alanine synthetase, cytidine deaminase, thiopurine methyltransferase, CYP1A1, CYP1A2, CYP2A6, CYP2A7, CYP2B6, CYP2B7, CYP2C8, CYP2C9, CYP2C17, CYP2C18. CYP2C19, CYP2D6, CYP2E1, CYP2F1, CYP3A3, CYP3A4, CYP3A5, CYP3A7, CYP4B1, CYP7, CYP11, CYP17, CYP19, CYP21, CYP27, glutathione transferase alpha, glutathione transferase theta, glutathione transferae mu, glutathione transferase pi, methylguanine methyltransferase, 3-alkylguanine alkyltransferase, 3-methyladenine DNA glucosylase, DNA dependent protein kinase, catalytic subunit of DNA-PK, DNA binding subunit of DNA-PK Ku-70 or Ku-80 subunit, KARP-1, Poly(ADP-ribose) polymerase, Fanconi Anemia genes A, B, C, D, E, F, G, and H, ERCC-1, ERCC2/XPD, ERCC3/XPB, ERCC4, ERCC5, ERCC6, XPA, XPC, XPE, HHR23A, HHR23B, uracil glycosylase, 3-methyl adenine DNA glycosylase, NF-kappa B, XRCC4, XRCC5/Ku80, XRCC6, XRCC7, glutathione-X-transferase, I-kappa B alpha, HSP70, HSP27, and 9-oxoguanine DNA glycosylase.

20

131. A method for identifying a potential patient undergoing transplantation for treatment with an inhibitor active on at least one but less than all alleles of an essential gene, comprising the step of:

25

identifying a patient undergoing an allogenic bone marrow transplantation in which the donor tissue contains at least one alternative allele of an essential gene different from the alleles in somatic cells of said patient.

WO 98/41648 PCT/US98/05419

386 232/116

132. The method of claim 131, wherein said donor or said recipient is homozygous for an alternative allelic form of an essential gene that is not present in the other of said donor or said recipient.

133. A method for treating graft versus host disease in a patient receiving allogenic bone marrow transplantation, said method comprising the step of

5

10

15

20

25

administering to said patient at least one allele specific inhibitor specific for at least one but less than all of the allelic forms of an essential gene in a population, wherein said inhibitor inhibits stimulation of the donor immune system, and cells of the said patient comprise an allelic form of said gene not present in the donor bone marrow.

134. The method of claim 133, wherein said allele specific inhibitor is selected by identifying at least one alternative alleles of an essential gene present in the donor tissues but absent in the normal somatic cells of said patient; and

selecting a said inhibitor active on a said alternative allele of an essential gene present in said donor tissues but absent in the normal somatic cells of said patient.

- 135. The method of claim 134, wherein said at least one inhibitor recognizes both alleles of said essential gene that are present in said donor, but not both alleles of said gene that are present in said patient.
- 136. A method for enhancing engraftment of an allogenic bone marrow transplant, comprising the step of administering to a patient receiving said transplant an allele specific inhibitor which kills or suppresses the patient's bone marrow but not the donor bone marrow, thereby providing space for engraftment of the donor cells within the marrow cavity.
- 137. The method of claim 136, wherein the allele specific inhibitor is selected by

WO 98/41648

5

10

15

20

25

identifying alternative alleles of an essential gene that are present in the recipient but not the donor marrow.

- 138. The method of claim 137, wherein said allele specific inhibitor recognizes both allelic forms of the essential gene that are present in the recipient, but not both allelic forms of the same gene that are present in the recipient.
- 139. A method for treating or preventing chimerism in allogenic bone marrow transplantation, comprising

selectively killing or suppressing proliferation of the patient's own cells without toxicity to the donor cells by

administering to a patient receiving said transplantation at least one allele specific inhibitor active on at least one but less than all alternative alleles of a gene vital for cell growth or viability, wherein said inhibitor targets the allelic form or forms of a gene in bone marrow of said patient but does not target at least one allelic form of said gene in the donor bone marrow.

140. A method for treating cancer in a patient receiving allogenic or autologous transplantation, comprising the step of

administering to said patient at least one allele specific inhibitor which kills or inhibits the growth of cancer cells without toxicity to the transplanted marrow.

141. The method of claim 141, wherein said transplantation is autologous transplantation and said at least one allele specific inhibitor is selected to be active on the allele of an essential gene remaining in the cancer cells due to LOH in patients whose normal somatic cells are heterozygous for said essential gene, but not on the alternative allele of said gene present in said normal somatic cells,

whereby said administration enables continuing therapy of cancer without suppression of the transplanted marrow.

WO 98/41648 PCT/US98/05419

232/116

142. The method of claim 140, wherein said transplantation is allogenic transplantation and said allele specific inhibitor recognizes both alleles of said essential gene that are present in the recipient, but not both forms of the said gene that are present in said patient.

5

143. A method for eliminating malignant cells from transplanted marrow during autologous transplantation of a patient heterozygous for an essential gene, comprising

10

contacting cells from harvested autologous bone marrow ex vivo with at least one allele specific inhibitor active on at least one but less than all alternative alleles of said essential gene, wherein said inhibitor targets an allelic form of said gene present in cancer cells of said patient but does not target an alternative allele of said gene present in normal cells from said autologous bone marrow,

wherein said gene has undergone LOH in cancer cells of said patient.

15

- 144. The method of claim 143, wherein said autologous bone marrow is harvested from said patient prior to high dose radiation or chemotherapy.
- 145. The method of claim 143, further comprising the steps of:

20

a. identifying one alternative allele of an essential gene remaining in the cancer cell due to LOH in patients who are heterologous with two different alternative forms of the essential gene in normal cells of the autologous bone marrow;

25

- b. cultivating said autologous bone marrow ex vivo in the presence of an allele specific inhibitor that inhibits the allele that is present in the cancer cells, but not the heterologous allele that is present in the normal bone marrow.
- 146. The method of claim 143, wherein said autologous bone marrow is contacted with a plurality of said allele specific inhibitors.

WO 98/41648

PCT/US98/05419

389

232/116

- 147. A method for separating a first cell from a mixture of cells, comprising the steps of:
- a) providing an allele specific binding compound which binds to at least one but less than all alleles of a gene, wherein a said allele of said gene expressed in said first cell is not expressed in other cells of said mixture of cells or is expressed in other cells in said mixture of cells and not in said first cell;
- b) contacting said mixture of cells with said binding compound under conditions such that said binding compound binds to said allele and not to non-target alleles; and
 - c) separating bound cells from unbound cells.
- 148. The method of claim 147, wherein said mixture of cells comprises normal somatic cells and cancer cells from a patient, said first cells are said normal somatic cells, and said first cells express a said allele deleted in said cancer cells due to LOH of said gene, comprising

separating said normal somatic cells from said cancer cells.

- 149. The method of claim 147, wherein said allele specific binding compound is an antibody or antibody fragment.
- 150. The method of claim 147, wherein said binding compound is attached to a solid support.

20

15

5

10

Target Gene Summary Table
Dihydropyrimidine Dehydrogenase
Chromosome 1p22-1q21
VARIA950

heterozygosity	+				SD % in blecks and chinese										peulu				
Protein		Cys/Arg	Met/				ozygostty								pe not detar		1	s genotype	
	Comments			These are	11 bases		56% = Locus Heterozygostty	ernnic e racial Gruo a≃Asian (olher) ogsårah	esh=Ashkenazi	.x Hese	ban Sk	anic n	an nese	pr=Puerto Rican	empty box - genotype not determined			Other populations genotyped: None	
	35 36 Hel%	TT TT 11%	%6 ¥7	AG 35%	CC 77 77 38%		%95 " "	a=Asian	A=4sh	o=Black c=Chinese	cu=Cuban g=Greek	h≠Hspanic Findian	k≕italian j≕Japanese	pr=Puert	.ambty		į	Nog.	
Genotypes of 36 unrelated individuals	12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34		44 44 44 44 44 44 44 44 44 44 44 44 44	* * * * * * * * * * * * * * * * * * *	20 20 21		3 3 3 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	Other SSCP polymorphisms: #			. Mary a dame a beautiful a second	Sequence nomenciature and nombering nom-	McBride, O.W., Podschun, B., Schnackertz, K.D., and Gonzalez, F.J. "cDNA Ctorsing and Chromosome Mapping of Human	Ditydropyrhridine Dehydrogenase, an Enzyme Associated With S-Fluorouracii Toxicity and Congenital Thymhre Uraciunia.	Journal of Biological Chemistry, 269 (37) 23192-23196	(₹55.)		Validation Status:	
99	Bess 1 2 3 4 5 6 7 8 9 10 11 12 1			W W W W W W W W W W W W W W W W W W W	W W W W W	C,T & & & C TT TT TT TT C C C C C TT TT TT TT C C C C C TT TT		Sequence around polymorphism*	TGCAACTCTGTGTTCCACTTC	TGCAACTCTGCGTTCCACTTC	ATTCAAAGCAATGAGTATCCC	ATTCAAAGCAGTGAGTATCCC	CCCACTCTTTGCTGTGCACAT	CCCACTCTTTACTGTGCACAT	TGTGCACATACGGGCTCTGAC	TGTGCACATATGGGCTCTGAC			boid rucleotide is the polymorphic base
	Location	+			- 1	ър 3937		Allele	166 T	166 C	577 A	577 G	3925 G	3925 A	3937 C	3937 T			*bold rucle
	Deliner Doir		DPD1a-DP0Zb	DPD10-DPD2s	DPD9a-DPD10b	OPD9a-DP010b		豊	VARIA500.2.1	VARIA500.2.2	VARIA500.3.1	VARIA500.3.2	VARIA500.1.1	VARIA500.1.2	VARIA500.4.1	VARIA500.4.2			

10/30/96

Target Gene Summary Table Thymidylate Synthase Chromosome 18p11.32 VARIA250

Race Specific	L Tuonity	wide distribution	wide distribution	wide Statibution	Probably rare												7	 		7	
Race	1000	8	8	8	8	_	٦									peul					
Protein		3'UT	3.01	5.6	tvr33hla	zygostły		s Surveyed:								e not determ		denotybed			
	Comments	s complé binge de .		by commission brange do-	So her deaded only in	= Locus Heterozygostty		Ethnic & Racial Groups Surveyed	(other)	kenazi	8	E	je S	8	pr=Puerto Rican w=White	empty box a genetype not determined		Other populations denotyped			
\vdash	Z ier	5.3%	\leftarrow	-	$\overline{}$	28% =		thule &	a≍Asian (other) ar≃Arab	esh=Ashkenazi h=Black	C=Chinese	cu=Cuban g=Greek	h=Hispanic i=Indian	t=Italian j≕Japanese	pr=Puerto	empty t		ther	None		
	35 36 1	ł	: 5					ĺШ		1 69 1	<u> </u>	0 6	<u> </u>	= -=	<u>a. s</u>	•		ار) <u>z</u>		
	32 33 34 3				AT AT M. M. AT AT TT M.	1	-	Γ				Γ			·			Γ		\neg	
	132		: {	31	-		-						has th	s)	ınction	Gene.			cifically		
	28 29 30 31			٤١ : ٤١ :	2	‡	3	*	1 "				cession	indaries	and F.	Pase 84.			y spec		
	2 128 12		<u> </u>	٤١ : ١	2 - -	+	1	*1	-				This ac	ğ X	tural	le Syn 77-202			acts b	İ	
	3,6		ដ	2	74 F	\pm	3	į	į				969	ntron/e	Stre	n Thymidylate Syntha 265: 20277-20284			uracil	lase.	
duals		3 3	8 8	۲ ۲	2	1	1 1	Short					2 00	uding h	(1990	년 왕			-fluore	Synd	
slenblylbri beteleren 30 %			<u>ਇ</u>	8	14	$^{+}$	•	Sept 6	Office Socie polymorphisms:				Sequence from: GenBank accession # D00596 (This accession has the	genomic sequence, including introderon boundaries.)	Seno, Ayusawa, D., (1990) Structural and Functional	Analysis of the Human Thymidylate Synthase Gene. J. Bishorical Chamietry 265: 20277-20284.			Validation: The cytotoxic drug 5-fluorouracii acts by specifically	inhibiting thymidylate synthase.	
Potelo	יופור פרוביים	707	7 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	<u>ছ।</u>	T.	+		9	ָ ברי				Sequence from: GenBank access	sequen	yusaw	10 th			on: otoxic	thyn	
1		=	된	2	AT AT AT	#			tuer o				equen enBan	anomic	eno. A	nalysis	ologic and a second		Validation: The cytotox	hibiti	
	S	14 15 16 17 18 19 20 21	원 원	2	X	+		[[<u> </u>			Ľ	<u>и о</u>	<u> </u>	2 0	<u> </u>	<u>-</u>	12	> ⊢	<u>.5</u>]	
	101	=	FI	হ হ	11 47	\pm		Г							- T		- [- 1			
1	- 1	12 13	3 S	<u>ا</u>	AT TA MA AT TT	\downarrow				F	Ţ	9	ŋ	Ę+	-	A	A			the polymorphic base	
		2	ह ह	2	2	1	4 E E		polymorphism*	ATAT	TAT	CTA	CTA	rAGI	rAGI	3660	3660			orphic	
	ŀ	•	81 E1	SG AA AA	<u>ا</u>	\dashv	3		ymor	AGG	AGG	GGA	GGA	TTA	TTA	CTG	CTG			polyn	
		7	8 보	۲ ۲ ۲		-	1			CGA	TGA	AAA	GAA	AAG	TAG	TAC	CAC				
		\$	7	94 94	E	\dashv	•		aron	AGCT	AGCI	AGA	AGA.	TTI	LTT	SCAC	SCAC			eotide	
		7	E 2	\$ 92 94	AT TT AT TT AA		•		Sequence around	CAAAGGAGCTCGAAGGATATT	CAAAGGAGCTTGAAGGATATT	TCTAAAAGAAAAAGGAACTAG	TCTAAAAGAAGAAGGAACTAG	ATGAACTTTAAAGTTATAGTT	ATGAACTTTATAGTTATAGTT	GGAGCTGCAGTACCTGGGGCA	GGAGCTGCAGCACCTGGGGCA			*bold nucleotide is	
	_	~ 8	ୃଷ୍ଟ	Y O Y	× 2	9	-		Sec	CAA	CAA	TCI	ŢŢ	ATG	ATG	GGA	GGA			•po	
		Base	Ü	Ž	A,T	2	_		_		1	<	(0)	<							
		Location	1140	1210	1571	276		,	Allek	1140 C	1140	1210 /	1210 G	1571	1571	276 T	276 C				
		Ш	54a	Ste	rp3	_			**		1	1		,	50.3.2	50.4.1	50.4.2				
		Primer Pair	T53b-T54a	153b-TS4a	TS3c-rp3				<u></u>	VARIA250.1.1	VARIA250.1.2	VARIA250.2.1	VARIA250.2.2	VARIA250.3.1	VARIA250.3.2	VARIA250.4.1	VARIA250.4.2				

Target Gene Summary Table Threonyl-tRNA Synthetase Chromosome 5p13-cen VARIA302

Prolein Race Specific Heterozygosity	ellord Corrections	اق م	Î	10 to	= Locus Heterozygosity	oups Surveyed:								empty box a genotype not determined	ne denotyped.	none	
A manual of the state of the st		2 1	3	TT 25%	* ** 47% = Locus H	Ethnic & Racial Groups Surveyed:	a=Asian (other)	ash=Ashkenazi h=Black	C=Chinese	g=Greek	h=Hispanic ⊨Indian	it=Italian ⇒Japanese	pr=Puerto Rican	*empty box = gen	the franchis	none population	
	26 27 28 29 30 31 32 33 34	GG AG GG GG GG AG	GA GA GG GG GG GG GG GG GG GA GA GG GA GA			3	Other SSCP polymorphisms. E 12				Sequence from: GenBank accession # M63180	Cruzen,M.E. & S.M. Arfin (1991) Nucleatide and	tRNA synthetase reveals extensive homology to the	Escherichia coli and yeast enzymes. J. Biol. Criem. 1266: 9919-9923.		Validation: Multiple other tRNA synthetases have been proven	essential for cell survival.
Gen	Base 1 2 3 4 5 6 7 8 9 10 11 12 13	GA 66	A.G. 66 66 66 66 64 66 66 66 66 66	T T T T T T T T T T T T T T T T T T T			Sequence around polymorphism*	CTACTCGCCCGGAAAATTCC	CTACTCGCCCAGAAAATTCC	TTAAAGATGCGATTGGGCGGT	TTAAAGATGCAATTGGGCGGT	TGCCAAAGTCTGAAATAGGTC	TGGCAAAGTCCGAAATAGGTC				bold nucleotide is the polymorphic base
	Location	bp 1608	bo1755	bp 2395			Allele	1608 G	1608 A	1755 G	1755 A	2395 T	2395 C				"bold nuc
	Primer Pair	Thr3b-Thr4	THES. THEM	TARS54-6a			#0	VARIA302.1.1	VARIA302.1.2	VARIA302.2.1	VARIA302.2.2	VARIA302.3.1	VARIA302.3.2				

Target Gene Summary Table TATA Associated Factor 2H Chromosome 11p15.2-15.5 VARIA520

Race Specific	SON of Blacks.				
	Location ne		reyed:	de termined	ityped:
	Comments	w a 22%=Locus Helerarydoulty	Ethnic & Racial Groups Surveyed a-Asian (other) an=Arab ash=Ashkenazi b=Black c=Chinese	u=cuban g=Greok h=Hispanc i=Indian j=Japanese p=Japanese p=Puerto Rican w=While *ampty box = genotype not determined	Other populations genotyped:
	35 36 Het% GA AA 22%	w w # 22%=Loc	Ethnic & Racial a=Asian (other) ar=Arab ash=Ashkenazi b=Black c=Chinese	cu=cuban g=Greek h=Hispanic i=Indian i=Halian j=Japanese p=Purft Rican w=White	Other popu
Genotypes of 36 unrelated individuals	5 26 27 28 29 30 31 32 33 34 GG GG GG GG GG GG GG GA	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	Other SSCP polymorphisms: # %	Sequence from: GenBank accession # U13991 Jacq, X., Brou, C., Lutz, Y., Davidson, I., Chambon, P., Jand, L. Tora (1994) Human TAFII30 is present in a distinct TFIID complex and is required for transcriptional activation by the estrogen receptor. Cell 79: 107-117. (Note: the numbering in the GenBank accession and the Cell 19:107-117 paper diter by two nucleobles; the	Validation: Other TATA associated factors (TAFs) have been proven essential for cell growth.
Genot	Base 1 2 3 4 5 6 7 8 9 10 11 12 13 14 G G G G G G G G G G G G G G G G G G		Sequence around polymorphism TGAAGGGCACAGGCTICCGGCA TGAAGGGCACAGCCTICCGGCA TGAAGGGCACAGCCTICCGGCACA		
	Location 554		Allele 554 554		
	Primer Pair TAF6-TAF2		1D# VARIAS20.1.1 VARIAS20.1.2		

Target Gene Summary Table Ribonucleotide Reductase, M1 Subunit Chromosome 11p15.5 VARIA200

	Cue	Constynes of 36 unrelated individuals		Location	Race Specific Helerozygosity
	01 6 6 1 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35	36 Het% Comments		
Location	24 27 W 25 W	NC NC NA CC NA CC NA			50% in Blacks
bp 1037	NG AG GG AA	AA AG GG	AG 40% polymorphisms are esparated by		SO% in Asians
bp2419	A.G M M M M M M M M M M M M M M M M M M M	W W W W W W W W W W W W W W W W W W W		3. UT	SON in Asians
bp2717	77 TT TT TT XT	AT TT AT TT T		3 UT	
bp 2724	19, 710	3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	" 1 58% = Locus Helerozygosity	ozygosity	
	1 4 B 70 4 4 6 0 B A A B B B A A B B B B A A B B B B B				
		Other SSCP polymorphisms: # %	Ethnic & Racial Groups Surveyed:	ips Surveyed:	
Allele	Sequence around polymorphism*		ar=Arab		
1037 C	CAACACAGCTCGATATGTGGA		ash=Ashkenazi b=Black		
1037 A	CAACACAGCTAGATATGTGGA		c=Chinese cu=Cuban		
2410 A	ATTTAAGGACAAGACCAGCAG	Sectionce from:	g=Greek h=Hispanic		
2410 G	ATTTAAGGACGAGACCAGCAG	GenBank accession # X59543	i=Indian it=Italian		
2419 A	CAAGACCAGCAGCTAATCCAA	Parker, N.J., Begley, C.G. and R.M. Fox (1991) Human	j=Japanese		
2419 G	CAAGACCAGCGGCTAATCCAA	M1 Subunit of Riobonucleotide Reductase: cDNA	w=While		
2717 T	GTTAATGATGTTAATGATTTT	Sequence and Explession in Summand 27 Procession Nucleic Acids Res. 19; 3741-3741.	emply box = generype not amply		
2717 A	GTTAATGATGATAATGATTTT				
2724 TB		Validation:	Other populations genotyped	s genotyped:	
VARIA200.5.2 2724 T10	ATGATAATGA (T) 10AAACTCATAT+	Hydroxyurea is a cytotoxic drug which specifically	No.		
	*bold nucleotide is the polymorphic base	binds and inhibits fiboritational reduction			
r after ba	Alumber after parends indicates length of homopolymeric repeat				

Target Gene Summary Table Ribosomal Protein S14 Chromosome 5q23-q33 VARIA326

Race Specific heterazygosity	50% in Whites					mined	ÿ
Protein changes	Silent	zygosity	s Surveyed			e not delet	genotype
Hel% Comments	44%	w w w 44 % = Locus Helerozygosity	Ethnic & Racial Groups Surveyed: a=Asian (other) ar=Arab	asn# Asnkenazi b=Black c=Chinese cu=Cuban	g=Greek h=Hispanic =Indian it=Hallan	-Japanese pr-Puerto Rkan w=White •ampiy box = genolype not delermined	Other populations genotyped:
Genotypes of 36 unrelated Individuals	12 13 14 15 16 17 18 19 20 21 22 23 24 22 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 20 20 20 20 20 20 20 20 20 20 20 20	CC	Other SSCP polymorphisms: # %		Sequence from: GenBank accession #'s M13934 &M13641 (genomic and	Rhoads, D.D., Dixit,A. and D.J. Roufa (1986) Primary Structure of Human Ribosomal Protein S14 and the Gene That Encodes It. Molecular and Cellular Biology 6: 2774-2783.	Validation: The poison emetine inhibits ribosome function by specifically interacting with RPS14.
Genol	Base 1 2 3 4 5 6 7 8 9 10 11 12 13 14	A.G 600 600 KG NG NG NG NG 000 600 600 600 NG	Sequence around polymorphism*	TTTCTGGCAAGGAAACCATCT TTTCTGGCAAAGAAACCATCT			*bold nucleotide is the polymorphic base
	Location	183	Allele	183 A			
	Primer Pair	rpS1-rpS2	#01	VARIA326.1.1			

Target Gene Summary Table Replication Protein A, 70 kDa Subunit Chromosome 17p13.3 VARIA401

				Slandy Individuals			
					Comments	Protein	Heterozygosity
1	l per tion	358	2 3 4 5 6 7 8 9 1		Marin & been of	100	11% in Caucasians
Primer Pair	Location	3		AC AN CO AN AC AN AC AN AN CO AC AC AC CO CO CO CO CO AC CO AC CO AC	E	Siloni	
RPA70.1-RPA70.2	-6	ठ। ठ	5			la351thr	ela351thr 44% in Caucasians
RPA7014-RP704f	1120	AG A	AC AA AA AA AA AA AA AG AG AA AA	AC AA A	rare	eer352phe	
RPA7014.RP704	1124	C, T				silent	21% in Swedes
RPA7014 RP704	1125	<u>ن</u> 1				silent	50% in Blacks 44% in Aslans
RP 703aa-RP 704c	1874	10	THE CONTROLLED THE THE THE THE	11 11 CT 11	2050	3.01	
RP 703c-RP 704a	2046	12, 13			MCD-in 4 berns of 2048	3.01	50% in Gaucadans
RP703c-RP704s	2050	T,C	CT CT CT CT CC CC CT TT CC CC	בו בס		3.01	75% in Blacks 50% in Caucadans
RP7036-4RP70	2297	දී පී	67. 87. 84. 67. 67. 9. 9. 67. 8. 69. 5.	0.5.9.9.9.9.9.9.9.9.9.9.9.9.9.9.9.9.9.9.		3.01	
RP7036-4RP70	2341	٧G	9999	%82	= Locus Heterozygostty	Apsob	
		لـــــــــــــــــــــــــــــــــــــ	2 to 4 to 4 d 4 d 4 d				
						٢	
į	Allella	Sec	Sequence around polymorphism*	Other SSCP Polymorphisms: 10# % Ethnic & Racial Groups Surveyed.	Sura year	·	
10,000		¥	ATG GTOGGOCAGCTGAGOGAGG	ar-Arab ash-Ashbanazi			
VARIA40112	A 1-0	¥	ATG GTOGGOCAACTGAGOGAGG	D:Black			
VARIA4012.1	1120 A		CTTGATGGACACATCCGGGAA	Sequence from:			-
VARIA401.2.2	1120 G		CTTGATGGACGCATCCGGGAA	GenBank accession # M63488			
VARIA401.3.1	1674 T		TCCAGGAGICTGCIGAAGCIA	ha-Hispanic hardware B and T 1 Kally (1991)			
VARIA401.3.2	1674 C						
VARIA401.4.1			GACTAAGCAA (1)2 CCI CCCI CGI+	stranded DNA-binding subunit of human replication			
VARIA401.4.2	2046 T3		AACCAATICTICCTCGTGCG	lion. w=white	handming to be a section of		
VARIA401.5.1	0000		A GCANTECCOCTEGTGCG	J. Biol. Chem. 266: 12090-12090.		7	
VARIA401.5.4	2297 C8		GTGGTGACCA (C) ATOCCOGCTC		lyped:	<u></u>	
VARIA401.6.2	2297 C9		GTGGTGACCA (C) ATCCCCGCTC	Validation:	in Swedes		
VARIA401.7.1	2341 A		TCAGCGGGGCAAGCTGAGAAG+	_	***************************************	_	
VARIA401.7.2	2341 G		TCAGCGGGGGGAGCTGAGAAG+			Ì	
		· po		ese			
+ The number after the parends indicates the length of the	er the parent	ds indicate	is the length of the homopolymeric segment.	Put			

Target Gene Summary Table Replication Protein A, 32 kDa Subunit Chromosome 1p35 VARIA402

Location Race Specific Heteroxygosity	S'UT 25% in Caucasians			zygoslty		ps Surveyed:	-								pe not determined		genotyped:		
16 Het & Comments	l			"1 11% = Locus Heterozygosliy		Ethnic & Racial Groups Surveyed:	a=Asian (outer)	ash=Ashkenazi b=Black	c=Chinese	g=Greek	h≖Hispanic	i=Indian	j=Japanese	pr=Puerto Rican	empty box = genotype not determined		Other populations genotyped:	None	
Genotypes of 36 unrelated Individuals	56 56 16 05 67 56 56 16 05 67	3				Other SSCP polymorphisms: # %					Sequence from:	GenBank accession # J05249	Frdile 1 F. Wold, M.S. & T.J. Kelly (1990). The	primary structure of the 32-kDa subunit of human	replication protein A. J. Biol. Chem. 205: 3177-	orus.		Validation: RPA has been proven essential for mammalian DNA	replication in vitro and for yeast viability.
Genol	Base 1 2 3 4 5 6 7 8 9 10 11 12 13 1	GA ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~			0 1 4 6 N 4 4 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		Sequence around polymorphism*	CCCCAGACCCGCACCTTCTCG	CCCCAGACCCACACCTTCTCG										*bold nucleotide is the polymorphic base
	Location	bp 40					Allele	40 G	40 A				_ _						
	Primer Pair	RPA32 1-RPA32 2					#0	VARIA402.1.1	C 1 CD 7 1 2	**************************************									

Target Gene Summary Table RNA Polymerase II, 220 kDa Subunit Chromosome 17p13 VARIA500

Location	Base 1 2 3 4 5		Genotypes of or mineral and in the second of		Chambes	115071701313
tion	_		15 10 10 10 10 12 12 12	5 36 Heth Comments	_	
		2	17 07 61 91 11 91 61	GC GG 22%	silent	38% in Caucasians
857	G.A GG GG GA GG GG	25 55 55 55 55 55 55	23 12 23 23 23 23 23 23 23 23 23 23 23 23 23	% 9 00	arg292cya	13% in Caucasians
1260	C,1 cc cc cc cc cc	20 20 20 20 20 20 20		CT CT 39%	slient	SO% in Caucasians
1348	C,T nc nc nc nc nt	20 20 20 20 20 20	22 23 23 23 23 23 23 23 23 23 23 23 23 2	cc 3%	Silent	
1544	C.T cc cc ct cc cc) 당	20 20 11 20 11 20 11 20 20 20 20 20 20 20 20 20 20 20 20 20	CC CC 31%	silent	50% in Blacks
1847	द्र ा व्यक्त वर्षा	20 20 20		CC CC 11%	silent	50% in Chinese
2678	C.T on on or or	25 25 25 25 25		c cc 31%	silent	75% in Chinese
3059	C,T cc ct cc cc	THE CT CC CC CC CC CC	23 23 12 23 12 12 12 12 12 12 12 12 12 12 12 12 12	CC CC 22%	sllent	36% in Caucasian
3827	C, Τ cc cc cτ cc cc	20 20 20 20	7 C C C C C C C C C C C C C C C C C C C	F	3.01	70% Aslan, 75% Black
6466	1 2 5	CC CC TT T		म म 6%	5 6	
6557	T,C TT TC TT TC T		3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	w # 83% = Locus Heterozygosity	Heterozygosli	ī
	4 4 4 *					
			Other SSCP polymorphisms: # %	Ethnic & Raci.	Ethnic & Racial Groups Surveyed.	. neken
Allele	Sequence aro	Sequence around polymorphism		ar-Arab		
857 G	GCGAGGGT	GCGAGGGTGGGGAGGAGATGG		ash=Ashkenazi	Έ.	
857 A	GCGAGGGI	GCACACACATGC		b-Black		-
١ _	TCAGCTGC	TCAGCTGCGCGCAATGAGCA		Cu-Cuban		
1260 T	TCAGCTGC	TCAGCTGCGGTGCAATGAGCA		g≂Greek		
1346 C	TGGTGGAC	TGGTGGACAACGAGCTGCCTG	Common from:	h=Hispanic		
1346 T	TGGTGGAC	TGGTGGACAATGAGCTGCCTG	seducine i o iii	it=Italian		
1544 C		GCCAACATGACCT	GenBank accession # X63564	= Japanese		
1544 T	CCATTGCT	CCATTGCTGCTAACATGACCT		pr=Puerto Rican	an	
1847 C	TGAATCTT	TGAATCTTAGCGTGACAACTC	Wintzerith, M., Acker, J., Vicaire, S., Vigneron, M. and C.	- mot pox a	waymile **moty box a genotype not determined	determined
	TGAATCTI	TGAATCTTAGTGTGACAACTC	Kedinger (1992) Complete Sequence of the Human			
2678 C	CTGAATAC	CTGAATACAACATCAAGT	RNA Polymerase II Largest Subunit. Nucleic Acids			
2678 T	CTGAATAC	CTGAATACAATAACTTCAAGI	Research 20: 910.			
3059 C	AGCTGCGC	AGCTGCGCTACGGCGAAGAUS				-
3059 T	AGCTGCGC	AGCTGCGCTATGGCGAAGACG				
3827 C	TGGGCCAG	TGGCCAGTCCGCTCGAGATG				
3827 T	TGGCCAC	TGGCCAGTCTGCTCGAGATG				
6466 T	CTGATGCA	CTGATGCAGATTCTTGTCTTG		Other popu	Other populations genotyped:	olyped:
6456 C	_	CTGATGCAGACTCTTGTCTTG	Validation.			
6557 T	TGTCCCCA	TGTCCCCAAATTGAAGATCCT	Linds the 220 kDa subunit and inhibits RNA	None		_
6557 C	16	TETCCCCAAACTGAAGATCCT	Polymerase II.			
1		and order order has	Tolymeras			

Target Gene Summary Table Glutaminyl-tRNA Synthetase Chromosome 3p21 VARIA305

Race specific heterozygosity	19% in Whites									rined			
Comments change		11% = Locus Heterozygosity	Ethnic & Racial Groups Surveyed: a=Aslan (other) araAsah	ash=Ashkenazi	D=Diack c=Chinese	g=Greek	h=Hispanic =Indian	t≠italian Babanasa	pr=Puerto Rican	empty box = genotype not determined		Other populations genotyped	
Genotypes of 36 unrelated individuals	7.11	# # # # # # # # # # # # # # # # # # #	Other SSCP polymorphisms: # % Ethnic 8 a=Asian a=Asian a		2-5	Sequence from:		Lamour, V., Quevillon, S., Dirlong, S., N'Guyen, V.C Itett		as a case of horizontal gene transfer. Proc. Nati. wey		Validation: Othe Multiple tRNA synthetases have been proven	essential for cell survival.
	C.T CT CC		Sequence around polymorphism*	TTAACAGGCACCGGCCCAGC	TTAACAGCATCGGCCCCAGC								*bold nucleotide is the polymorphic base
	Location 404		Allele	404 C	404 T								Pold nu
	Primer Pair Gin1-Gin2		#QI	VARIA305.1.1	VARIA305.1.2								

Target Gene Summary Table Sodium, Potassium ATPase, α1 Subunit Chromosome 1p13-p11 VARIA125

Name operation	Heterozygosity	50% of Blacks		25% of Whites		50% of Blacks															7	-			7
1001	Change	silent	slient	Asp740Glu	silent	silent	3 UTR	3 UTR	rygosity	eyed:									Paris and and	Cetamped			typed:		
	Comments									Ethnic & Racial Groups Surveyed:	, .	E						ue		empty box = genotype not geternured			Other populations genotyped:		
	6 Het%	A 11%	9 98	11%				3,%	28%	Ethnic & Racial	de	ash=Ashkenazi b≈Black	c=Chinese	cu≖Cuban g=Greek	h=Hispanic	ran:	t=Italian E-Japanese	pr=Puerto Rican	Thite	¥ pox			er popu		
	33 34 35 36 Het%	A AA	99 99	1	·	3 8	3 8	2 2	2	Ethn a=As	ar=Arab	ash=Ash b=Black	ن ا	cur-Cubar g=Greek	Ī	Findian	#=Italian	P=P	w≖White	Ē			O.		
Senotypes of 36 unrelated individuals	5 26 27 28 29 30 31 32	AN A		\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	11 11 11 11 11 11 11 11	22 22 23 23 23 23 23 23 23 23 23 23 23 2	25 25 25 25 25 25 25 25 25 25 25 25 25 2	22 22 23 23 23 23 23 23 23 23 23 23 23 2		Other SSCP polymorphisms: # %					Sequence from:	Genbank Accession #: Doods9	Kawakami K. Ohta, T., Nojima, H., and K. Nagano	(1986) Primary structure of the alpha-subunit of	human Na, K-ATPase deduced from cDNA sequence.	J. Biochem. 100: 389-397.			Validation:	Ouabain is a potent cytotoxic drug which inhibits Na.	K-ATPase by interactions with the a1 subunit.
The State of the S		2 3 4 5 6 7 8 9 10 11 12 15	AA AC CC AA AA AA AC AA AA AA AA	3	T.C 11 11 11 11 11 11 11 11 11 11 11 11 11	20 20 20 20 20 20	8	99 99 99 99 99 99 99 99 99 99 99 99	20 20 20 20 20 20 20 20 20 20 20 20 20 2		TOTTTTCACAAAATIGIGIIG	TCTTTICACCAATTGTGTG	TGGGGTCCACGTCT	TGGGGTCCACATCCACCATCT	CTGGCTCAGATGTGTCCAAGC	CTGGCTCAGACGTGTCCAAGC	TCGTATATGACGAAGTCAGAA	TCGTATATGATGAAGTCAGAA	GGGTGGAGAAGCAAACCTACT	GGGTGGAGAAAGAAACCTACT	TTAGCCCCCGTCCTGCACGC	TTAGCCCCCCATCCTGCACGC	TCCTGCACGCCGTGGAGCATC		*bold nucleotide is the polymorphic base
		Location	1059	1428	2538	3324	3375	3397	3408		Allele	1059	1428	1428	2538	2538	3324	3324	3375	3375	3397	3397	3408	3408	
		Primer Pair	F21-R19	F10-R20	F27-R28	F16-R12	F28-R27	F28-R27	F28-R27		#0	VARIA 1231.1	VARIA 125.11	VARIA 125 2.2	VARIA 125 3.1	VARIA 1253.2	VARIA 125.4.1	VARIA 125.4.2	VARIA 125.5.1	VARIA 125.5.2	VARIA 125.6.1	VARIA 125.6.2	VARIA 125.7.1	VARIA 1257.2	

Target Gene Summary Table Lysyl-tRNA Synthetase Chromosome 16q23-24 VARIA303

changes Patterns	31% in Whites	ser,thr 50% in Blacks	erozygosity	oups Surveyed:						empty box = genetype not determined	ns genotyped:	
36 Het% Comments	AA 19%	% 9 33	" 25% = Locus Haterozygosity	Ethnic & Racial Groups Surveyed: a=Asian (other)	ash=Ashkenazi	c=Chinese	cu=Cupan g=Greek	h=Hispanic i=Indian		empty box = gen	Other populations genotyped:	
Genotypes of 36 unrelated individuals	AG AA AG AG AG			Other SSCP polymorphisms: # % 2 3%				Sequence from: GenBank accession # D31890	Nonuca,N. Mitalina,N., Sazuka,T., Tanaka,A., Karwashayashi Y., Nagasa,T., Ishkawa,K., Set,I. E. S. Tabab. (1993). Prediction of the coding sequences of unidentified human genes. I. The coding sequences of 35 genes deduced	by analysis of randomy sampled CUNA consa stom numeri inmaking myabid cell line KG1. Unpublished	Validation:	essential for cell survival.
	1 2 3 4 5 6 7 8 9 10 11	20 20 20 20 20 20 20 20 20 20 20 20 20 2		Sequence around polymorphism*	AGCTGAAGAGGCCCTGAAAG	AGCTGAAGAGGCGCCTGAAAG	ACAGTTGGCAGTTCTGTCTAG	ACAGTIGGCACTTCTGTCTAG				*bold nucleotide is the polymorphic base
	Location	1798		Allele	89 A	89 G	1789 G	1789 C				*bold nuc
	Primer Pair	Lys3-Lys4		#Q.	VARIA303.1.1	VARIA303.1.2	VARIA303.2.1	VARIA303.2.2				

314/98

Target Gene Summary Table Glutamyl Prolyl-tRNA Synthetase Chromosome 1q32-q42 VARIA300

i	_	Ű	Genotypes of 36 unrelated Individuals		Protein	Race Specific
Base	-	2 3 4 5 6 7 8 9 10 11 12 1	10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36	35 36 Het% Comments	changes	Heterozygosity
ð	ပ္ပ	0 00 00 00 00 00 00 00 00 00 00 00 00 0	သ သ သ သ သ သ သ သ သ သ သ သ သ သ သ သ သ သ သ	7.2	pro821his	25% in Blacks
3	<u>ي</u>			13% tumer Bras)	silent	
2,	_			1/12 total	his969tyr	
A,G		A A BO AN AN AND AN AND AND AND AND AND AND AN	AN A	A 24% 10/42 total	l lle971val	
٧C		AG GG AG AA GG AG AA AA GG AG AG AG AG A	IN GG AN GG GG GG AG AG AG AG AG GG GG AN AN AG AG AG AG AN AG AN AG AN AN	41% 17/41 total	silent	50% in Japanese
త		GG GG AA AG AG AG	GC AG GG AG AA AA AG AG AG AG AA GG AG AA GG AG A	1 51% 21/41 total	1 3'UT	70% in Aslans
ઢ		GG GG AN NG AG AG	GG AG GG AG AN AG AG AG AG AG AN GG AG AN GG AN AG		3.01	70% in Aslans
	3	4 5 m 4 4m m 4 6 m a 4 4 4	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	a a a a a a a a a a a a a a a a a a a	fund(mind mon	
	Set	Sequence around polymorphism	Other SSCP polymorphisms: # %	Ethnic & Racial Groups Surveyed	ups Surveye	.;
	₹	AATTCTGAACCTGCTGGTTTA		ar≕Arab		
	\$	AATTCTGAACATGCTGGTTTA		b=Black		
	2	TCATCACAAAGTCAGAAATGA		c=Chinese cu=Cuban		
	2	TCATCACAAATCAGAAATGA		g=Greek		
	ō	GATTGAATACCATGACATAAG		n=nspanic i=Indian		
L	Q	GATTGAATACTATGACATAAG	Sequence from: GenBank accession # X54326	It=Italian i=Iapanese		•
L	A	ATACCATGACATAAGTGGCTG	Fett, R. and R. Knippers (1991) The Primary Structure	pr=Puerto Rican		
	AT	ATACCATGACGTAAGTGGCTG	of Glutaminyl-tRNA Synthetase. J. Biol. Chem. 266:	w=White "senotype not determined "empty box " genotype not determined	ype not dete	rmined
L.	₹	AATGGGTACAATCACAGAG				
	₹	AATGGGTACAGTCACACAGAG	"Note: See Kalser,E., Hu,B., Becher,S., Ebenhard,D., Schray,B., Baach,M., Harneister,H., and R. Kriepear (1994). Genomics 19: 280-280 for the			
ļ	8	GATACAGACCGTTTTATGATT	correct name of the gene. (The Fett and Knippers paper is mistaken.)			
l	ð	GATACAGACCATTTTATGATT				
١.,	A	AAGTCACACAGGACAATTATT	Validation	Other populations genotyped:	amquus s	ż
	₹	AAGTCACACAAGACAATTATT	er tRNA synthetases have been proven	None		 ;
	Bold airch	Rold michaelds is the notworthic hash	essential for cell survival.			

Target Gene Summary Table Initiation Factor elF-5A Chromosome 17p13-p12 VARIA351

		Geno	Genotypes of 36 uprelated Individuals		_	Race Speculic
Primer Pak	I ocation Base	1 2 3 4 5 6 7 8 9	10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36	He 1%	Location	Heterozygosity
9153.0	623	SS	GG GG GG GG GG GG AG AG AG AG AG AG AG A	GG 37% the spice acceptor	3.UT	44% Caucasian
ALE 11E-4	1932	21 30 30 31 30 30 30 30 30 30 30 30 30 30 30 30 30	TC TC CC TT	cc 62%	3.UT	present in all groups
			3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	#1 63 % = Locus Heterozygostty	zygoslty	
10#	Allele	Sequence around polymorphism*	Other SSCP polymorphisms: # %	Ethnic & Racial Groups Surveyed: a=Asian (other)	s Surveyed:	
VARIA351.1.1	623 A	GGCTCCCAGGATGGCGGTGGT		ash≖Ashkenazi ash≖Ashkenazi		
VARIA351.1.2	623 G	GGCTCCCAGGGTGGCGGTGGT		b=Black c=Chinese		
VARIA351.2.1 1012 C	1012 C	CCCTGTTGCCCATAGCCCTTT	Sequence from:	cu=Cuban		
VARIA351.2.2 1012 T	1012 T	CCCTGTTGCCTATAGCCCTTT	GenBank accession # U17969 (This accession contains the franchic sections of introduced buildings indicated	h=Hispanic		
			See Variagents annotated cDNA sequence for sequence numbering used in this table.	Italian		
			- safety Colombia Colombia	F=Japanese pr≂Puerto Rican		-
			Adelling, A., Wolli, I., Nappelio, Coupering, I., Isaber, S., and D. Bevec (1995) Identification of a new member of the	w=White rempty box = genotype not determined	not determine	-
			human elt-5A family. Gene 159: 283-284.			
			Validation: This is the only human protein which contains hypusine.	Other populations genotyped	genotyped:	
		*bold nucleotide is the polymorphic base	Inhibition of hypusine formation is cytostatic.			

Target Gene Summary Table Cytidine Triphosphate Synthetase Chromosome 1p34.1 VARIA259

Race Specdic		1/4 Chanese	1/1 Cambodian	2/4 Chinese								_		_						peul					_
Location	Locarion		3 UTR	3 GR					i i	en very serie										not determ			notyped		
Comments	Comments	Low frequency	Low frequency	Low frequency				w w p 11% alocus Helerozygosky	Paragraph and Children Cont.	other)	1							Rican		empty box = genotype not determined			Other populations genotyped:		
¥1001	2013	× 9	3%	%8				1		eninic o nacial e=Asian (other)	ar=Arab _{ash=} ashkanasi	b=Black	c=Chinese	cu=Cuban	y-Green h≃Hispank	-Indian	it≖italian I Ispapose	p=Puerto Rican	w=White	by po			er po		
- 13	*	≨	ខ	8				1		¥=9	ar=Arab	b=8	짇	3 6	2 E	Ĭ.		7	*	Ē			oth		
H	33 34 35 36	≨ 0	8	95 95	-	-	-	1	٦			_	_	۲	_						_		_		_
:	=	AN A	8	8	+	-	+											Mar			ļ				
[~	2	20 22 22 22 22 22	99 99 99 99 99 99 99 99 99 99 99 99 99				,		_,								Yamauchi, M., Yamauchi, N. and M. Meuth (1990). Molecular	<u>la</u>						
	<u> </u>	₹ ¥	5	9	-	╀	\vdash	1 1	ŀ	*								5.	nctio	9	İ			spect	
	29	۲ ۲	<u> </u>	9		\dagger	+	1										(199	Š	seudi			ŀ	4	
	2 2	٤	ပ္ပ	9					ľ	#!			İ	-				age.	9119	E e				osine	
	5	2	8	9	-	-	+	P 		::			-	- [Ž	1Se 9	man .	22			ykcyt	
	2	Y	8	9	-	+	\dagger	+-		E			١				,	pug	theta	2 2	2095			enter	
<u> </u>	2	Š	Š	1		İ	I	8	ľ	른						£174		z	Psy		66			ges	
칅.	긺	2	8	8	3	+	+	1-1		Ĕ				Ì		ä		品	ı CI	≝. 5.	7			ر خ	
탉	7	<u>₹</u>	X	1 5	3	+	+	-	- }	od					Ë	5	5	Yam	Iuma	¥ LC	EMB			Per c	0
盲	9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30	¥		1	3	İ	İ	-	1	Other SSCP polymorphisms:			-		Sequence from:	Chromback According # X52147	2	Σ	cloning of the human CTP sythetase gene by functional	complementation with purified human metaphase	chromosomes. ЕМВО J. 9: 2095-2099.		=	Cells are polsoned by cyclopentenylcytosine, a specific	Inhibitor of CIPS
5	-	¥¥	t	1	5	1	Ţ	1:		S					Jenc	ş	<u> </u>	햠	jo 6	e me	1050		Validation:	210	5
98	딁	ž	ÿ	,	31 21	1	+			otte					Sequ	9		'ama	ioni	dwo	hron		la lid	Sillo.	
s of	9	<u>۲</u>	٤	1 5	3	\dagger	\dagger	1-1	1	<u>-</u>	_			t	•,		_		U	3	<u>. </u>	j	2	<u> </u>	=_
Genotypes of 36 unrelated Individuals	=	\$	٤	1	3	Ţ	Ţ																		
al-	픩	*	٤		Vin 20, 20, 20, 20, 20, 20, 20, 20, 20, 20,	+	+	┿╣	ī					-1		\neg		- 1	- 1	_		1		_	
ŏ۲	7	*	1	3 3	3	+	\dagger	+=										- 1						86	
	Ξ	\$	Ł	3	3	Ţ	1	E 5		Ę		ď	ای	ای	ا_		ļ							oolymorphic base	
-	릐	3	1	3 3	3	1	4	4		Ę	2	3TC	Ş	Š	ទ	5								<u>a</u>	
}	9	3	1 5	1 1	3	+	+	1 3		olymorphism	CAAGGTCA	CAAGGTCA	ő	TGGGAACC	CACCTTGT	CACCTTGT		ļ						SE	
İ	-	2	1 8	3	8	I	1	-		poly	2	Ş	ATG	ATC	3TC	2	1					$ \ $		8	
	9	3		3	8	I	1	3		Pu	¥	Ye	ဗ္ဗ	GIG	ğ	Š								£	
1	4 5	A M M M M	2	ارد اد	20 20 20 20	+	+	+:		Sequence around po	GTCAGTTCCAATT	GTCAGTTCCAGT	CAGAACATCGCGATGGGAACC	CAGAACATCGTGA	TGTCCCCATCGGT	TGTCCCCATCAGT					İ			"bold nucleotide is the p	
	3	1	1	3	8	+	+	+-		92	AGI	AGT	A	\$	ပ္ပြင္ပ	띯			ı					90tic	
	2	*	I	31	ક	I		4			310	GTC	18	Y.	101	2								E C	
닏	-	_	7			+	+	B		Š														plo	
	Base	9 V	1	5	<u></u>	1		_		_	L			_					_					٥٠	
	Location	576	2000	2093	2135					Altele	576	576	2093	2093	2135	2135									
	Primer Pair	200	2	F11-K1	F11.R11					#0	VARIA259 1 1	VARIA259 1 2	VARIA259.2.1	VARIA259.2.2	VARIA259.3.1	VARIA259.3.2									

Target Gene Summary Table Cysteinyl-tRNA Synthetase Chromosome 11p15.5 VARIA301

Protein Race Specific	Ť	pro622leu 50% Black	50% Chinese		a theory	ups Surveyed:						-		empty box = genotype not determined		s genotyped.	ozygosity (98/267)	
	6 Het% Comments	44%			 w w.l 44% = Locus reletazyyosky	Ethnic & Radal Groups Surveyed:	a=Asian (other)	ash=Ashkenazi	b=Black c=Chinese	cu≓Cuban g=Greek	h=Hispanic i=Indian	#=Italian	pr=Puerto Rican	*empty box = genoth		Other negativities denotyped	Swedes: 37% heterozygosity	
Genotypes of 36 unrelated Individuals	10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 Het%				3 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	1	Other Sacr polymorphisms. # 70 and				Sequence from. GenBank accession # L06845, and	Cruzen, M.E. and S.M. Arfin (1994) Nucleotide and Deduced Amino Acid Sequence of Human Cysteinyl	IRNA Sequence. DNA Sequence 4: 243-248	The Cruzen and Artin paper is the source for nt 1-2048. Genbank accession at 05645 contains a further 423 nt at the 3' and, but facks the	19 consecutive A residues after 2029 reported in Cruzen and Arfin.		Validation: Multiple other tRNA synthetases have been proven	essential for cell survival.
Genot	Base 1 2 3 4 5 6 7 8 9 10 11 12 13 14	t			0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		Sequence around polymorphism*	ACATCCTGCCGAGCTTGGGG	ACATCCTGCCTGAGCTTGGGG									*bold nucleotide is the polymorphic base
	tocation	1,730	_				Allele	1739 C	1739 T									
	Dritmer Park	73 65	55				ID number	VARIA301.1.1 1739 C	VARIA301.1.2 1739 T									

Target Gene Summary Table Alanyl-tRNA Synthetase Chromosome 16q22 VARIA304

Race Specific	Herozygosity																		
	Profesh	Silent					Ygoshy	s Surveyed:										enotyped	
	Comments						u u u u u u u u u u u 67% = Locus Heterozygosky	Ethnic & Racial Groups Surveyed:	eeAstan (other) ar=Arab	esh=Ashkenazi b=Black	956	k and	_ =	FJapanese		empty box = genatype not defermined		Other populations genotyped:	
	10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 CT 34 35 36 Hers.	ट्राटमट्रामट्राट्र ८५८ ६४%					57%	Ethnic	ar=Arab	ash=Ash b=Black	or Chinese cur Cuban	g=Greek h=Hlspanic	indian H≈itelian	FJapanese	w=White	ещеру		Other	
	36	8						<u> </u>	~				<u> </u>				j	0 2	
	٤	ु	\dashv			_		_			1						,		
	F:	7		-	_		-						٠,	ا ≽	6 축			_	
	32	Ĕ			_		1						Shiba K., Remaster, T., Suzuki, N., Nichols,R., Plotz, P.,	Noda, T. and P. Schimmel (1995) Human alanyl-tRNA	synthetase: conservation in evolution of catalytic core and microheltx recognition. Biochemistry 34: 10340-			8	-
	3	ី៤					•						g	Į,	34.			Multiple other 18NA conthairses have been provided	
	30	5					3	14					و مر	aga				5	
	8 29	ಿರ	_	_			*							nan ,	ist,				3
	7 21	্যক্ত		\dashv				324					Shiba,K., Remaster, T., Suzuki,N., Nichols,R.,	쿠 :	, Me			2	}
	9	: ∪ ::-	-	-	_			١					z	8	oct o			غ ا	;
	25	17		-		\vdash	3 2 4	E				١	3 3	65	(A)				
ğ	12	5	\neg	\dashv	-	_	-	ş				}	SE	ne !	<u> </u>			1	
	23	E		\dashv			-	ğ			ļ		. H	Ē	grit			5	, <u>Ş</u>
	22	ंड					*	통				l	ig a	3				2	5
2	21	11					\equiv	8				E	E CER	ا نه	2 4			9	
	20			\Box			1 1 2 2	Other SSCP polymorphisms:				Sequence from:	2 2	E .	že.			نِي إِ	essential for cell survival.
Genotypes of 36 unrelated individuals	1.5	ij		_				S				e :	# ×	⊢ }	ig ig	6		Validation:	ial
٩	=	<u> 8</u>		_		\sqcup		쿌				200	يَّةٍ عَ	å å	E E	10349		lida Air	Sen
5	9	۲		\dashv			\dashv	ĺδ			ļ	ο c	5 05	ž	<u>a</u>	₽_		Z Z	ë
	5		-				and h can h i												
5	=	i.	\dashv	-		Н	H												
Š	13	ाः	-		-	Н			_	Т		T			_	_			
ان	12	E		\dashv	-	Н			1	A			l			1		1	
	Ξ	F			\neg	М	3	1	၂ပ္ပ	122			1			1	1		
	10	t					4	¥	JA S	34			l		ļ				
	9	Ľ	\Box				\$	8	ij	ğ			1			1			
	•	8	\dashv]				ofvenorablem*	GCTCGGACCA	GCTCGGACCA			l			1)ase
	, 7	្ត		_		Ш			၂ ဗွ	8			l			[اقا
-	5 6	g	\dashv			Щ		1	Į.	18					İ				[꽃
	-	್ *ಕ						Š	၂ ပ	၂ပ	l		1					1	힐
	-	E.		\dashv	-	Н	1 1 1	Sequence around	CTGGCTGACCAT	CTGGCTGACCAC									ļ
	2	ಿಕ	_	\dashv		\dashv	\exists	5	5	5			ĺ					1	4
	-	ច		_		\vdash	7	8	၂ ဗ	100					1			1	Ę
	Basse	C,T						"	្រី	15									ide is
	Location	bp 1013						Allela	1013 T	1013 C						-		-	*bold nucleotide is the polymorphic b
	_									ŀ		_					L		ا م
	Primer Pair	Ala 1a-Ała 2						ğ	VARIA304.1.1	VARIA304.1.2		[

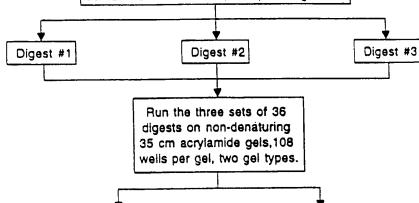
Fiz.2

SSCP Overview

PCR amplify gene from 36 cell lines:

- 1. Purify RNA from 36 cell lines.
- 2. Use reverse transcriptase to make cDNA from all cell lines.
- Do PCR with radioactive nucleotides or kinased primers to amplify and label overlapping .2 - 1.5 kb fragments spanning target gene cDNA.

Set up three different restriction digests to cut the radiolabelled PCR products from all 36 cDNAs into 100-400 base pair fragments.



Gel #1: 5.5% Acrylamide, 0.5X TBE buffer Gel #2: 8% Acrylamide, 10 % Glycerol, 1X TTE buffer

Dry gels, expose to X-ray film and inspect autoradiographs to identify variant DNA bands.

Select variant cDNA samples and use DNA sequencing to determine sequence of variant alleles.

Use agarose gels, SSCP or DNA sequencing to determine genotype of additional individuals in order to better determine allele frequencies in different population groups.

Fig. 3 Chromosome 1 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
36.	0172	110.	24	0.22	Breast	cross surgical
36	D1Z2	37	15	0.41	Breast	AJHG 45:73
36 36	D122	18	9	0.5	Differences	GT 12 - 7 - 7 - 7 - 7 - 7 - 7 - 7 - 7 - 7 -
36	D1Z2	20	1	0.05	Endocrine	CR 52:770
36	0172	7	7	1	, Neuroblastom	CRC55-5366
					ā	
36	D15243	43	10	0.23	Breast	CR 55:1752
36	D19243	20	5	0.3	Endocrine	
36	D1S243	14	14	1	Neuroblastom	CR 55:5366
					a Neuroblastom	**************************************
36 :-	D18243	. 36	. 9	0.25	"Mentoprasion:	
	210043	8	7	0.88	Neuroblastom	GCC 10:275
36	D1S243	8	,	0.00	a	
36-35	D1980	9	- 0	0	Brein	(4)
36-35	D1S80	14	1	0.07	Brain	CR 54:1397
36-35	D1580	34	16	0747	Brasin	7012250690155
36-35	D1S80	17	4	0.24	Breast	GCC 12:16
Unknown	D1580	74	22	0.3	Breast	MATE OF CONTROL OF
36-35	D1S80	63	20	0.32	Breast	CR 54:4274
36-35	D1S80	40	8	0.2		GC0:143+9
36-35	D1580	13	10	0.77	Neuroblaston	GCC 10:275
30 22					а	
36-35	D1S80	38	9	0.24	Meuroblaston	CR255:5681
					<u> </u>	CR 54:6265
Unknown	D1S80	19	2	0.11	Testis Testis	0:9:2245
Unknown	D1580	17	***************************************	0.12	Brain	AJP 145:1175
36.3-35	D1S76	34	16	0.47	Breast	GR 53 4356
36.3-35	D1576	41	4	0.1 0.16	Breast	GCC 12:16
36.3-35	D1S76	19	3	0.16	Breast	CR 54:4276
36.3=35	D1576	38	15	0.88		n GCC 10:275
36.3-35	D1S76	17	15	0.80	a	
Ga known	D1577	21	- 10	0.48	Brain	AND 145 LLTE
Unknown	D1S77	19	3	0.16	Breast	GCC 12:16
Unknown	DIS77	18	4	0.72	PK (opiniore all	665 10 274
Unknown	D1577	6	2	0.33	Stomach	BJC 73:424
Onknown	019253	17	3	0.18	Leukemia	erces below
36	D1S47	32	3	0.09	Breast	CR 51:1020
36		15	1	0.077	Colon	(#;3474/2HF
36	D1547	17	12	0.71	Colon	CR 50:7232
36	D1547		7	0.29	Melanoma	PNES 8514614
36	D1S47	31	7	0.23	Neuroblasto	m GCC 10:30
- -					а	
36	0)19214	43	\$ (\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	0,19-		CR 55 1/52
36	D1S214	11	10	0.91		om GCC 10:275
					a	

Chromosome 1 - p Arm

36	D15216	13	0	0	Storach	BUC 75 424
Unknown	D1S160	17	9	0.53		AJP 11145:11
Unknown	D19160	21	5	0.24	Liver	
Unknown	D1S160	34	8	0.24	Neuroblastom a	
*Unknown	*D19160	41	22	0.54	***************************************	eneritations
Unknown	D1S244	36	9	0.25	Neuroblastom a	
36	D18450	37	8	0.22	Breast	
Unknown	NPPA	1	0	0	Testis	GCC 13:249
Unknown	PGD	10		0.1	Testis	Engowia I/A C
36	D1S228	40	5	0.12	Breast	CR 55:1752
36	CD19228	7	5	0.71	Neuroblasion a	
36	D1S228	31	7	0.23	Neuroblastom a	
3.6	D13228	8	1	0.12	9tomach	3.p(=):3.5x(1/2/23
Unknown	D1S170	19	5	0.26	Liver	CR 54:4188
-Unknown	· -D1S170	36.		0.19	Neuroblestom a	
Unknown	D1S170	33	16	0.48	Ovary	BJC 75:1105
Unknown	D1S94	19	12	0.63	Colon	(017/50/7/EX
Unknown	D1S94	8	4	0.5	Neuroblastom a	
Unknown	D1S94	36	9	0.25	Neuroblaston	/GCC110:30.
C11.03.0					3	
35	D15199	50	9	0.18	Breast	CR 55:1752
35	D19199	30	4	0.13		CRC56:197
35	D1S199	14	13	0.93	Neuroblaston a	
35	.D1S199	4	2 .	0.5	Neproblasto	.GCC2101275
35	D1S199	9	0	0	Stomach	BJC 73:424
36.1+p34	ALPL	17	2	0.12	Colon ()	CR.52:285
36.1-p34	ALPL	2	1	0.5	Endocrine	CR 52:770
36.1=p34	ALPL	17	4	0.24	Melanomay	2025 6 6046
36.11	D15112	1	1	1	a	n CR 55:5366
Unknown	DISI12	20	1	0.05	Neuroblasto	(6.782.35
Unknown	FUCA1	15	5	0.33	Brain	AJP 1145:11
Unknown	FUCAL	13	6	0,46	Melanoma	## 15 E S E S E S E S E S E S E S E S E S E
Unknown	FUCA1	14	0	0	Testis	GCC 13:249
Orknown	D19234	10	- 8	0.8	Neurobleeto	eran in eran
36.2-36.1	FGR	12	2	0.17	Brain	CR 54:1397
36.2-36-1		7	0	0	\$ - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	enanca Buddia
36.2-36.1	FGR	4	2	0.5	Endocrine	CR 52:770
36.2-36.1	FGT	1/2	6	0.45	Ovary	

Chromosome 1 - p Arm

Unknown	D1S63	39	4	0.1	Testis	CR 54:6265
Unknown	019247	2	1.0	0.5	Neuroblastom	Committee of the
	**************************************				ā	en 53.1000
36.2-34	D1S95-96	74	20	0.27	Breast	CR 53:1990
Unknown	D1S96	17	11	0.65	Neuroblastom	
36.2-36.12	D1S95	19	2	0.11	a	0 7.1103
	D1S96	18	O	0	Neuroblaston	
UDDIOWII	21020	•			a	
32	D1S7	105	43	0.41	Breast	CR 54:4274
32	D1S7	46	13		Breast	ZKelejesty sektossá
32	D1S7	28	26	0.93	Colon	CR 50:7232
32	D187	24		WINDS AND DESCRIPTION OF THE PARTY OF THE PA	Endocrine	DIS 64-1083
32	D1S7	13	1	0.08	Liver	BJC 64:1083
32	D1\$7	50	15	1	Liver	CR 55:5366
32	D1S7	6	6	1	g Mediopiasco:	- CR 55.5500
32	0157.	14	5	0.36	Pancreas	THE CHARLES
32	D1S7	31	3	0.1	Stomach	HG 92:244
32	D1\$7	45	14	0.531	Stomach	STATE OF THE PARTY.
32	D1S7	31	3	0.1	Stomach	BJC 73:424
32	D197	- 30		003	Testis	GCC=13:249
Unknown	D1S233	19	5	0.26	Head&Neck	CR 54:1152
Unknown	D1S233	4	. 2.	0.5	â	s GCC 10:2752
Unknown	D15241	4	3	0.75	Neuroblasto a	m GCC 10:275
Unknown	D15201	35	0	C		GR 549.49.56
Unknown	D15201	19	1	0.05	Head&Neck	CR 54:4756
Unknown	D15201	8	3	0.38	Neproblasto	m GCC 10.275
	7.00				8	
Unknown	D1S201	12	3	0.25	Stomach	BJC 73:424 CR=50:5784=1
35-32	D1857	15	1		**Brein	AJP 1145:117
32	D1\$57	26	12	0.46	Brain Brain	GR44 9: 65 /2
35-32	*D1857			0.06	Breast	GCC 2:191
35-32	D1S57	18 73:	1 1-5	0.06	Breast	riordenia (E) BL
35-32 35-32	D1S57 D1S57	43	Α.	0.09	Breast	CR 50:7184
35-32		B1	36	0.44	Breast	701 3
35-32	D1S57	3	2	0.67	Breast	CR 53:3804
35-32	01557	4.4	6	0.51	C Press	
35-32	D1S57	19	6	0.32	Breast	CR 51:6194
35-32	DIS57	23	5	0.22	Breast	cle each by a line of
32	D1S57	74	23	0.31	Breast	CR 53:1990
32	D1957	52		0.02	00-7-1-7	CCC 9.119
35-32	D1 S 57	6	0	0	Cervix	GCC 9:119 BUC 64-475
35-32	D1857	180	40	0.22	*Colon	CCG 48:167
35-32	D1S57	22	2	0.09	Colon	CCG 40.10,

PCT/US98/05419

Chromosome 1 - p Arm

35-32	DEST	16		***************************************		
35-32	D1S57	12	0	0	Colon	N 331:273
	TO BE SEED AND ADDRESS OF THE SECOND	16		0.06	e ja jaros sa kaja se	
32	D1S57	12	8	0.67	Endocrine	CR 52:770
55-Y-	01857	15.	6	0.4	Podoczane	CR 54:2996
32	D1S57	27	8	0.3	Esophageal	CR 54:2990
3/2	D1857	14	1 2 2	-0.07	Kidney	CR 51:89
35-32	D1S57	22	1	0.05 0.18	Liver Lung	CR JI. 09
35-32	01957	28	5		Neuroblastom	TAX TAX DESCRIPTION OF THE PARTY OF THE PART
32	D1S57	2	2	1	a	erano nu sa sa sa
77	701957	14	1		Ovacy	***************************************
35-32	D1S57	18	7	0.39	Ovary	0 7:1059
35-37	DIS57	- 4	0.2	C C	Rancieas	CR 52:2419
35-32	D1S57	20	2	0.1	Sarcoma	CR 52:2419
32	D1957	5		1.6		G 5:134
35-32	D1S57	17	0	0	Testis	2000200
444.32	D1S57	92		0:05 0.05	Testis	CR 54:6265
32	D1S57	37	2	0.03	Uterus	OTHER CHAINE.
35=32	01957	8		0.09	Uterus	CR 51:5632
32	D1S57	11	1	0.09		Goc Michael S
:Enknown	D19255	14	7.2		a -= '2''	
Unknown	D1S255	5	4	0.8	Stomach	BJC 73:424
Unknown	D19186	25	7	0.28	Liver	CR 54:4188 CR 53:1990
32	MYCL1	74	26	0.35	Breast	GGC 12(128
37	MYCL1	••••	365	0.44	Breast	HG 85:101
32	MYCL1	152	55	0.36	Breast	RG 05:101
32	MYCLI	59	23	0.39 0.12	Breast Breast	AJHG 45:73
32	MYCL1	17	2	0.12	Breast.	
32	WACTI	16	2	0.1	Colon	CR 52:285
32	MYCL1	20	2	0.1	colon	CONTRACTOR OF THE
32	NYCLI	20	1	0.11	Endocrine	CR 52:770
32	MYCL1	9 20	4	0.11	Designation (Co.	interestication
32	** ** BYCLI		8	0.67	Endocrine	CR 52:770
32	MYCL1	12			and a state of the	A CHARLES
32		18	2	0.11	Liver	JJCR 81:108
32	MYCL1	27	1 × 12 × 12		Karaja pa i Tapangana	(m) (m) (m) (m) (m) (m) (m) (m) (m) (m)
	MYCL1	5	0	0	Lung	CR 54:5643
32 22	MYCEL	3				~0.43(\$746353;65 <i>0</i>
32	MYCL1	57	12	0.21	Lung	0 10:937
32	Wichi Water	20			State of the Contract of the	ENTTHE #12
32	MYCL1	2	1	0.5	Lung	CR 54:5643
Unknown	W. V. LYGISIS	9		0.72	Neurobless	on services
				0.00	077277	BJC 75:1105
32	MYCLl	41	9	0.22	Ovary	500 .5.0200

Chromosome 1 - p Arm

			A Company of the Company			ov spineter a
77	MYCLIU	13	4	0.31	Ovary Ovary	GO 55:245
32	MYCL1	17	4	0.24	OVALV	gene and the
2	TWO IS	77.			Sarcoma	CR 52:2419
32	MYCL1	9	0	0	Salcona	Contract of
37	WYCE-L	4	0		Testis	CCG 52:72
32	MYCL1	1	0	0		7740 (1976) (1
12	Tyen C		0	0		CR 54:4294
32	MYCL1	20	1	0.05	Uterus	era e e e e e e e e e e e e e e e e e e
Unknown	(CIPIVAL)	23	3			CR 56:197
34.2-32.2	D1S190	23	3	0.13	Cervix	
¥.2-57.2	DISTRO.		1	0.337	- a	Constitution
Unknown	D1S193	7	2	0.29	Neuroblastor a	n GCC 10:275
	DISZLI	42		1,311	a description	
Unknown	D1S211	5	3	0.6		n GCC 10:275
					а	(Flemostick)
aunknewn.	DIS197	12.	7	0.58	Keuloulasto	
			-	0.31	Stomach	BJC 73:424
Unknown	D1S197	16	5	0.31	Breas	Sample of City
372	01562	76	19.	0	Colon	CCG 48:167
32	D1S62	15	0	1		STATE OF THE STATE
32	D15.62	2	2		Breast	Unknown
Unknown	D1S162	0	5	0.26.	Liver	(GESSA) /4188
Unknown	D1S162	19	5	****		om GCC 10:275
Unknown	D1S200	12	7	0.58	а	
				0.45	Nettroplast	m (CR 25 5 5 68)
Unknows	D15200,	33	5		a	200 m
		74	22	0.3	Breast	CR 53:1990
Unknown	D1S15	/ 4		0.25	Endocrane	
Unknova	DISI5	24	6	0.25	Testis	CR 54:6266
Unknown	D1S15		9	0.55	Piration .	AND THE STREET
pter-22	DISZI	18	AND DESCRIPTION OF THE PERSON	0.27	Breast	CR 53:199
pter-22	D1S21	74	20	6	Direct Block	
H1-pter	D1571	10	0	0.08	Endocrine	CR 52:770
31-pter	D1521	12	1			XXX TEXT CONTRACT
AN TOTAL	DISZLE				Brain	AJP 1145:
31-pter	D1S17	19	8	0.42	Breast	1000
0.00	0.517	8		0.12	Breast	CR 51:102
31-pter	D1S17	5	0	0		as var Greatly
300-22	1111 TO 1111	74	272			CR 52:770
pter-22	D1517	4	3	0.75	Endocrine	
77	CIETA	9	777.77.			GCC 13:9
31-pter	D1S17	13	2	0.15	Endocrine	GCC 13.9
200	0.01S17	19 -	31			CR 53:19
pter-22	D1S18	74	20	0.27	Breast	
pres-22	DISTS	5		0.67	Salde-Frie	A PARTY AND IN

Unknown	D1S203	14	6	0.43	Neuroblastom a	GCC 10:275
	D15246	11	0	0	Slomach	CHICAR TRAIN
Unknown Unknown	D1S209	15	7	0.47	Neuroblastom a	
Ninknown	D18159	16	3	0.019	(figures)	\$6.61.75X \$11.55
Unknown	D1S219	8	0	0	Stomach	BJC 73:424
	015464	44	- 11	0,74		(et land the street,
21	D1S216	14	13	0.93	Neuroblastom a	CR 55:5366
21_	01S216	-8	6	0.5	Newsonlaston	
pter-31	D1S2	12	7	0.58	Brain	AJP 145:1175
pter=31	0182	1	0	0	Breast.	(1000) YEAR OF THE STREET
pter-31	D1S2	74	19	0.26	Breast	CR 53:1990
pter=31	DISZ	16		0.19	Melanoma	2145.00.458
31	D1S500	33	8	0.24	Breast	CR 55:1752
7.32	:D1S430	39	10	028		(A) (A) (A) (A) (A) (A) (A) (A) (A) (A)
Unknown	D1S207	15	8	0.53	a	n GCC 10:275
Muknown	D18207	. 14	9	0.14	e Barrieli	en recharge
pter-22	D1S16	74	22	0.3	Breast	CR 53:1990
opter=22	D1S16	11		0	«Cervix	AND POST STATEMENT
pter-22	D1S16	6	2	0.33	Endocrine	CR 52:770
pter-22	D1316	24	4	0.17	Melanoma	PVIC 86.45.4
pter-22	D1S16	13	5	0.38	Testis	CR 54:6266
31	D15226	36	7	0.19	Breast	
Unknown	D1S167	9	1	0.11	Liver	CR 54:4188
Dokogyo	AF3	10	ō	0	Breast	AUHG, 45 - 7444
Unknown	AF3	26	6	0.23	Testis	CR 54:6265
Unknown	D15236	11		0.45	Neuroblasto	more south
						CR 53:1990
22-13	D1S10	74	19	0.26	Breast	CR 33.1990
, Unknown.	SEYMA	***************************************	(1)		100	CR 54:4188
21	AMY2B	16	5	0.31	Liver	- 17VE-3
215					Uterus	CR 54:4294
21	AMY2B	12	0	0	Promi	0.00
27-13	01919		(A)	0.02	Endocrine	GCC 13:9
22-13	D1S14	18	3	0.17	Endocime	
72-13	**D1514	25		9	Brain	AJP 145:1175
21-13	D1 S7 3	13	6	0.46		Complete Complete
(2) = 15)	01573	74	23	<u> </u>	Breast	GCC 12:16
21-13	D1S73	22	6	0.27	Breast	() () () () () () () () ()
	T DIST			0:26	Brain	AJP 145:1175
22-13	D1S9	8	6	0.75	Brain	2000000
222 - 19	DISS	74	73	0.31 0	Testis	CR 54:6265
22-13	D1S9	25	0	U 0.06	Colon	
	RAPIA	18		V.00		

PCT/US98/05419

Chromosome 1 - p Arm

	D1S418	39	8	0.21	Breast	CR 55:1752
13	DIS416	71		0.28	al-engle	
	NRAS	10	5	0.5	Endocrine	CR 52:770
13	NRAS	6	1	0.17	Descriptions	min Lystain - is
	NGFB	32	13	0.41	Brain	AJP 145:1175
13	NGFB	6	0	6	OFFICE STATE	eccione and Care is
30.13	NGFB	13	2	0.15	Breast	AJHG 45:73
13	NGEB	13	2	0.69	- Greage	Sale Trespersions
13	NGFB	18	3	0.17	Colon	IJC 53:382
13		5		0.2	Testas	Made and Alley 2
- 13	NGFB NGFB	16	0	0	Testis	CR 54:6266
13		10	0		Testis	grande and a library of
13	NGFB	3	0	0	Testis	CCG 52:72
13	NGFB	6	0		Uterus	
13	NGEB		19	0.26	Breast	CR 53:1990
22-13	D1511	74	19	0.20	Breast	Production of Arrest
21-Ngv	D1836	74	16	0.22	Breast	CR 53:1990
22-13	D1S13	74	i i	0.86	Endocadina	Media 42 20 731
722-13	DISLOT	7	6	0.86	Endocrine	CR 52:770
22-13	D1S13	7 8	10	0.36	Brett -	Section 12 of Continues
322.1=13	D1S64	36	1	0.03	Breast	JNCI 84:506
31-pter	Unknown		20	0.27	Breast	of Carrier of Control
32	015100-101	74	4	0.44	Breast	CR 51:1020
Unknown	D1S33	9 37	6	0.16	Colon	(
3,3-,5	<u>Onknown</u>	7444 A		0	Colon	CCG 48:167
Unknown	Unknown	14	0	0.17	Endocrine	coups is
Unknown	D15188	23		0.5	Endocrine	CR 52:770
Unknown	D1S19	4	2	0.5	Endocrine	5/2017
Unknown	PND	3	-	0.16	Head&Neck	CR 54:1152
Unknown	D1S252	19	3	0.19	HeadaNeck	\$100 CONTRACTOR (CANADA)
Опклочп	DISST-NGFE			0.05	Kidney	PNAS 92:2854
Unknown	D1S243-D1S228	22	1 0	0.03	Kidney	District Color by
Unknown	DISSECTIONS OF THE PROPERTY OF	6		0.09	Kidnev	CR 55:6189
Unknown	D1S:243-228	33	3	0.09	Live	and the contract of the second
33-35	Unknown	14 35			Liver	CR 54:4188
Unknown	D1S187	19	4	0.21 0.22		100000000000000000000000000000000000000
Whikaown	· SISOL	27	6	0.31	Liver	CR 54:4188
Unknown	ISO2	13	4	CANADA MARKANIA MARKA	DIVET	Waster Commence
GERMOND	D1S19	21			Melanoma	CR 56:589
Unknown	D1S:214-201-255	20	1	0.05 0.38	Melanoma	
Unknown	PND	13			Neuroblast	
Unknown	D1S220	20	10	0.5	Medicoras	
				0.64		entere de la constant
Jukcown	D15232	11.				
Unknown	D1S252	8	2	0.25	Neuroblas	tom GCC 10:275
UIKINOWII	013242	•	•		a	

26 / 214

Chromosome 1 - p Arm

Unkrown	D1997	18,,	C.	C	Neuroblasto	mt 0 / 1,1285
Unknown	GGAT2A07	28	3	0.11	Neuroblasto a	om CR 55:5681
*Hekonium	D1560	18		0.06	Cyary	
Unknown	D1S:162-175	14	1	0.07	Ovary	BJC 72:1330
Unknown	YMA-ET?	25	6	0.24	Overy	BJC 75:1105
Unknown	MTHFR	28	16	0.57	Ovary Prostate	6371-530
13-36	PND-D1S2-NGEB	11	0	0.33	Stomach	BJC 59:750
3.35	Unknown	7135	1886	0.26		

Chromosome 1 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
Unknows	019305	30	7	0.2	Cervix	Control (Con
CENTR	D1S305	14	1	0.07	Neuroblasto:	m CR 55:5366
Unknown	D1567	30		0.03	Brain	en in the state of
21	D1S67	74	7	0.09	Breast	CR 53:1990
lnknown	01567	1.5	2	0.013	Breagt	(A):
Inknown	D1S67	7	2	0.29	Cervix	GCC 9:119
	D1567	26	3	0.12	Esophageal.	e caración de la como de la como de la como de la como de la como de la como de la como de la como de la como d
Jaknowa	D1S67	14	1	0.07	Kidnev	CR 51:820
Unknown	D1567	6	-	0.17	Lune	(G:05/04/27);
Unknown	D1S67	3	3	1	Lung	CR 52:2478
Unknown	D1567	3	1	-	Lung	SPAPPIGE
Un known	33-1	17	5	0.29	Lung	CR 52:2478
Unknown	D1S67		3	0.29	Oversy	Maritin Carlottine
Unknown	•••••		***************************************	0.09	Ovary	IJC 54:546
21	D1S67	23 - 26	2	0.09	Tentis	
Unknown	D1667	***************************************		0.18	Uterus	GCC 9:119
Unknown	D1S67	22	4	9:12		and the second contract
21-23	MUC1	74		- 0	Breast	CR 53:3804
21-23	MUC1	7	0	AND DESCRIPTION OF THE PERSON	Control of the Contro	
21-23	MUCT	44	13	0.3	Breast :	CR 51:1020
21-23	MUCl	43	7	0.16	Breast	CR 51:1020
21-23	MUCI	21	T	0:33	Head&Neck_	CR 51:2926
21-23	MUC1	16	4	0.25	Stomach	GCC=13:249
21-23	MUCI	25	2	0.08	Tentis	
21	PEM-pMUC10	89	14	0.16	Breast	GCC 5:311
21	SPTAL	74	9	0.12	Hreast	CR 53 (1990)
21	SPTAl	6	2	0.33	Breast	GCC 12:16
.21	SPTA1	6	2	0.33	Breast	PN: 86:7204
21	SPTA1	22	2	0.09	Colon	CR 52:285
21,	·SPTA1	29		0.1:	Colon	CROS2528
Unknown	D1S176	17	1	0.06	Liver	CR 54:4188
22-2-5	ATPIBL	511	9	0.12	Breast	CR. 45 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
21-23	APOA2	6	0	0	Breast	GCC 2:191
21-73	APOAZ	18		0.22	OVALY	and the second second
21-23	APOA2	5	0	0	Testis	GCC 13:249
Vale Tax	AF0.92	26		100	Siferant .	eterri Financii
21-31	D1S61	74	10	0.14	Breast	CR 53:1990
N 77 C 18 N	ATE (3)	52	977	1.786		PROGRAMMA VIOLENCE
21-31	D1S61	39	8	0.21	Breast	GCC 12:16
21=0	DISEL	29		0.1	7,(0)000000	Contract Contract
Unknown	D1S75	14	0	0	Brain	AJP 145:117
Unknown	D1975 •			0.00	70.0	CONTRACT MINISTER
Unknown	D1S66	14	4	0.29	Esophagea	CR 54:2996
Unknown	D1566	- · · · · ·	0	0	Saycomav.	
23-25	AT3	19	0	0	Brain	CR 54:1397
23-25	TIES.	1.6			25-25-7	es de la compania de la compania de la compania de la compania de la compania de la compania de la compania de

Chromosome 1 - q Arm

23-25	AT3	14	1	0.07	Breast	AJHG 45:73
23-25	ATS	7	0	0	THE PERSON NAMED IN COLUMN TWO IS NOT THE OWNER.	26-4-26-10 PM
23-25	AT3	14	0	0	Colon	CR 52:285
23-25	AT3			0	Livers	**(##**(##)4** 3
23-25	AT3	22	1	0.05	Ovary	IJC 54:546
3-25.1	211.3	- 5	- 0	0	Overv	ACRES 11/27/24
23-25	AT3	27	0	0	Testis	CR 54:6265
23-25	ATO	- 8	2	0.25	_ Testis	GCC 13: 249
nknown	D1S238	22	4	0.18	Cervix	CR 56:197
1=32.1	F13B	9	0	0	Brain	CP 54 1397
1-32.1	F13B	15	0	0	Brain	CR 54:1397
1-32.1	F138	12		0.08	Endocrine	Constitution of the second
1-32.1	F13B	13	0	0	Uterus	CR 54:4294
***************************************	D1S65	18	0	0	37-15	Constitution of the second
Inknown Inknown	D1S65	18	5	0.28	Breast	GCC 12:16
************************	01965	6	Ü	0)	Esophages.	
Jaknowa Jaknowa	D1S65	16	2	0.12	Head&Neck	CR 52:1494
	D1365	15		0.7	Resides:	(01,441) (14,07407 <i>f</i>
or room	REN	11	0	0	Brain	AJP 145:117
12 or 42	REN	12		0.25	Stepse	98-79; «Lessifición»
Z:or 42.	REN	21	7	0.33	Breast	GCC 12:16
32	REN	G		€0.17	Breast	CB 53-1990
2 or 42	REN	12	2	0.17	Cervix	CR 49:3598
32 or 42	REN	16	-	0.06	Colon	CR552:285
32	REN	19	7	0.37	Colon	IJC 53:382
32 or 42	REN	8	C	0	Liver	PNAS 86:885
32 or 42	REN	14	0	0	Liver	JJCR 81:108
32 or 42	REN	- 4	D	0	Neuroblasi	om. CR#49:1095
32.or 42	NEN.	7			8	
32 or 42	REN	21	1	0.05	Ovary	IJC 54:546
32 or 42	***************************************		0	0	Prostate	(F=0.445(0)
32 or 42	REN	15	4	0.27	Stomach	CR 52:3099
32 or (2	REN	İ	9	-0.27	Testils	(e) (e) (e) (e) (e) (e) (e) (e) (e) (e)
32 or 42	REN	6	0	0	Uterus	CR 51:5632
32 01 42	D15249	12	C	0	Neimoblas	tom CR2555566
		100			1	64 6265
Unknown	LAMB2	13	1	0.08	Testis	CR 54:6265
Опклои п	01856	24		1:46		
Unknown	D1S58	27	7	0.26	Cervix	CR 54:4481
Unknown	731558	15	0	0.00	60.101	(eec-(15-16)
Unknown	D1S58	21	4	0.19	Testis	CR 54:6265
Unknown	DIS58	23.	5	0 7/4/	resets	18 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -
Unknown	D1S81	32	0	0	Brain	AJP 145:11
Unknown	D1581	39.		0.51	Breasta	7 COC 1974 I.G.
Unknown	D1S81	41	5	0.12	Breast	CR 53:435
***********************	D1561			0.05	10 miles (10 miles 10	A CONTRACTOR OF STREET
Unknown	D1S213	30	6	0.2	Cervix	CR 56:197

Chromosome 1 - q Arm

On enokin	erityki kar	1			engri nin asi	ൂരിലുകുന്നു. 🎉
Unknown	D1S74	11	4	0.36	Breast	GCC 12:16
William over	93-30-58		in article (at 100 miles)	$x_1(x_2) = x_1(x_2)$	SOTTIAL BA	_17:00 V=14:- 15
Unknown	D1S74	39	7	0.18	Cervix	CR 54:4481
Unknown	PA 58	(0)			o sanda na in eo	
32-44	D1S103	18	2	0.11	Ovary	BJC 69:429
Unknown	SOUTH TO SEE	4.4		6		
Unknown	D1S74	50	3	0.06	Tes tis	CR 54:3983
Unknown	DIEVA			0.05	775 (2 47)	\$160.00 PV (\$150.00)
Unknown	D1S8	31	2	0.06	Testis	GCC 13:249
Unichawa	Jables	31	7	0.07		३०(तल्ला=====≠≠≠€)ः 👪
21-23	Unknown	70	18	0.26	Breast	JNCI 84:506
21-24	# Unknown	75	16			4-17-17-17-17-28-17
Unknown	DF3	43	6	0.14	Breast	IJC 61:1
10 S-3	1 dinteriorne			0.00	e e an la compa	
2.14	Unknown	27	3	0.11	Colon	BJC 59:750
II. I strong	D/5102	A Dark	Carry San	e ប្រជុំមិន		A CAMPER NO.
Unknown	D1S215	11	2	0.18	Endocrine	CR 56:599
in and	A STATE OF THE STA			The state of the s	and the state of t	at fore it wishly a fe
Unknown	D1S304-212	43	6	0.14	Head&Neck	CR 54:4756
University.	015507=212	17		20-5FA	Readeneck	or yezhio
Unknown	Unknown	8	3	0.38	Liver	BJC 64:1083
42-43	Uplanaga	13		0-23	Liver	e a succession de
Unknown	Unknown	4	1	0.25	Liver	BJC 64:1083
Unknown	DIS:237=712	27	2	0.07	Melanoma.	CP 56:589
Unknown	APOA2-D1S:158-103	14	0	0	Ovary	BJC 72:1330
Unioneven	REN-D1981	44	9	0,39	Overv	CR351-2393
Unknown	Unknown	13	2	0.15	Pancreas	BJC 65:809
32-44	Buknowa	7	0	0	Pancreus :	
4.23	Unknown	6	1	0.17	Stomach	вјс 59:750
2.31-4	Unknown	10		\$ 0V-75	5 country	nt a biological services
Unknown	AGT	52	3	0.06	Testis	CR 54:3983
Unknown	AGIT		0	0	Testin	to (a), is possible.
Unknown	CR2	21	3	0.14	Testis	CR 54:6265
Unichowe	antenine :	27.0		0	Tent	son therewa
Unknown	D1S180	50	7	0.14	Testis	CR 54:3983
20.714.00	and the second				APTO SECTION	in the contract
Unknown	D1S235	39	4	0.1	Testis	CR 54:3983
ec Sjade	The state of the s	2869				

Chromosome 2 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
Unknown	D2S44	7	1	0.14	<u> Uterus</u>	GCC 9:119
Unknown	Unknown	11	1	0.09	Brain	CR 50:5784
Unknown	D2S44	7	1	0.14	Breast	CR-53:3804
Unknown	D2S44	74	6	0.08	Breast	CR 53:4356
Unknown	D2547	23	0	0	-Breast	CR 50:7184
23-15	D2S6	27	3	0.11	Breast	GCC 2:191
23-15	D256	22	2	0.09	Breast	JNCL 84:506
23-15	D2S6	42	5	0.12	Breast	CR 53:4356
23-PTER	TPO	50	21	0:42	Breast	BCRT 32:5
Unknown	D2S139	27	4	0.15	Cervix	CR 56:197
Unknown	D2S177	18	2	0.11	Cervix	CR 56:197
Unknown	D2S44	7	0	0	Cervix	GCC 9:119
Unknown	D2844	48	6	0:12	Cervix	CR 54:4481
Unknown	D2S48	26	3	0.12	Cervix	CR 54:4481
Onknown	APOB	7	0	0	Colon	CCG 48:167
Unknown	D2S44	236	37	0.16	Colon	BJC 64:475
Unknown	D2S45	14	0	0	Colon	CCG 48:167
Unknown	D2S155	11	2	C.18	Endocrine	CR 56:599
Unknown	D2S44	60	10	0.17	Esophageal	GCC 10:177
Unknown	D2S44	20	4	0.2	Esophageal	CR 54:2996
Unknown	D2S47	41	10	0.24	Esophageal	GCC 10:177
Unknown	D2547	30	2	0.07	Esophageal	CR 54:2996
Unknown	D2S162	Ž1	4	0.19	Head&Neck	CR 54:1152
Unknown	D2S166-149	15	0	0	Head&Neck	CR 54:4756
Unknown	D25166-149	20	1	0.05	Head&Neck	CR 54:4756
Unknown	D2S207-D2S131	21	0	0	Kidney	PNAS 92:2854
Unknown	D25207-D28131	6	0	0	Kidney	PNAS 92:2854
Unknown	D2S47	11	2	0.18	Kidney	CR 51:820
Unknown	D2S:207-131	32	0	0	Kidney	CR 55:6189
Unknown	D2S48	9	0	0	Liver	CR 51:89
13	TGFA	5	0	0	Liver	PNAS 86:8852
Unknown	Unknown	27	6	0.22	Lung	CR 54:2322
Unknown	D2544	7	2	0.29	Lung	CR 54:5643
Unknown	D2S44	4	2	0.5	Lung	CR 54:5643
Unknown	D2S44	22	11	0,5	Lung	CR 54:5643
Unknown	D2S47	19	1	0.05	Lung	CR 522478
12.	COBA	20	3	0.15	Owary.	BJC 69:429
Unknown	D2S44	23	9	0.39	Ovary	CR 53:2393
Unknown	D2947	11	0	0	Ovary	CR 51:5118
23-15	D2S6	31	7	0.23	Ovary	IJC 54:546
23-PTER	TPO	14	2	0.14	Cvary ::	BJC 69:429
Unknown	D2S1	14	1	0.07	Prostate	G 11:530
Unknown	D253-D296	6	0	0	Prostate	G,11;530
Unknown	D2S47	10	2	0.2	Sarcoma	CR 52:2419
Unknown	D2S123	13	1	0.08	Stomach	CR 55:1933
Unknown	D2S44	45	12	0.27	Testis	0 9:2245
12222						

Chromosome 2 - p Arm

Waltania .	E2549	31	5	0.16	Testis	0.9:2245
24	MYCN	2	0	0	Testis	CCG 52:72
24	MYCN	2	0	0 .	Testis	CCG 52:72
24	MYCN	2	0	0	Testis	CCG 52:72
13	D25101	21	0	0-	Uterus	GCC 9:119
Unknown	D2S44	7	1	0.14	Uterus	GCC 9:119
SUM		1272	191	0.15		

Chromosome 2 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
13	ILIA	20	0	0	<u> Uterus</u>	CR 54:4294
Unknown	D2S44	17	0	0	Brain	CR 49:6572
Unknown	D2644	17	0	0	Brain	CR 50:5784
Unknown	CRYG	8	1	0.12	Breast	GCC 2:191
Onknown	D2S44	51 🦸	7	0.14	Breast	GCC 4 r 1 1 3
Unknown	D2544	31	3	0.1	Breast	GCC 2:191
Unknown	D2544	49	5	0.1	Breast	CR:50:7186
Unknown	CRYG	9	1	0.11	Cervix	CR 49:3598
Unknown	D25172	28	4	0:14	Cervix	CR 55:1974
Unknown	D2S172	29	7	0.24	Cervix	CR 56:197
	CRYG	21	0	0	Colon	N 331:273
<u>Unknown</u> 35-37	D2S3	16	0	0	Colon	CCG 48:167
***************************************	D2S44*	32		0.03	Colon	CCG-48:167
Unknown	D2S54	8	0	0	Colon	CCG 48:167
Unknown	D2534		2	0.1	Endocrine	CR 56:599
Unknown	D23123	14	1	0.07	Esophageal	CR 51:2113
Unknown	D2855	13	0	0	Esophageal	CR 54:2996
Chknown	***************************************	20	3	0.15	Head&Neck	CR 54:1152
Unknown	D2S111	10	0	0	Head&Neck	CR 54:4755
Unknown	D2S163		4	0.2	Head&Neck	CR 54:4756
Unknown	D2S163	20	,	0.04	Kidney	PNAS 92:2854
Unknown	D25125	28	5	0.13	Kidnev	CR 51:820
Unknown	D2S44	38	0	0	Liver	CR 51:89
33-35	CRYP1	11	***************************************	0	Liver	CR 51:89
Unknown	D2S44	18	0	0	Liver	PNAS 86:8852
Unknown	D2944	4	0	0	Liver	CCG 48:72
p16-15	D2S5	4	0	0.28	Lung	CR 522478
Unknown	D2544	40	11	 0, 25	Neuroblas	
p16-15	D2S5	1	0	U	ma ma	CO CK 43.1030
			•	0.39	Ovary	CR.53:2393
Unknown	D2S3	23	. 9	0.14	Ovarv	CR 51:5118
Unknown	D2S44	29	4	0.2	Ovary	CR 50:2724
p16-15	D255	5		0.2	Ovary	CR 50:2724
Unknown	D2S50	10	0	0.11	Ovary	IJC 54:546
Unknown	D2S55	19	2	0.11	Ovary	BJC 69:429
Unknown	D2S72	16	6		wale with the control of the contro	CR 54:2761
Unknown	D2544	4	0	0 27	Pancreas Sarcoma	CR 52:2419
Unknown	D2S44	26	7	0.27	AND DESCRIPTION OF THE PARTY OF	HG 92:244
Unknown	D2S44	18	1	0.06	Stomach	LI 73:606
Unknown	D2S44	27	0	0	Testis	CR 54:4294
13	ILIA	20	0	0	Uterus	Ch St. Fest
SUM		744	86	0.12		

Chromosome 3 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
2.6	D3S17	12	10	0.83	Kidney	CR 51:1071
26	D3S17	7	7	1	Lung	GCC 1:240
Unknown	D3S1307	36	2	0.06	Esophageal	BJC 73:366
Unknown	D351317	31	10	0.32	Kidney	BJC 69:230
Unknown	0391317	12	3	0.25	Stomach	CR: 55:1933
25	D3S18	19	9	0.47	Kidney	CR 51:1071
25	D3S18	i		1	Lung	GCC_1:240
	D3S1038	21	6	0.29	Esophageal	CR 54:6484
14	D351038	37	5	0.14	Esophageal	BJC 73:366
···	D3S1038	5	0	0	Kidney	GCC 12:76
14	**************************************	40	19	0.47	Kidney	BJC 69:230
14,	D351038	6	5	0.83	Lung	JAMA 273:55
14	D3S1038	-1	1		- Lima	JAMA 273155
13	D391038		3	0.12	Uterus	CR 54:4294
14	D3S1038	25	3	0.32	Cervix	CR 56;197
Unknown	D3S1263	22	4	0.67	Kidney	CR 51:4707
Unknown	D3S651	6	3	0.17	Lung	CR 52:873
Unknown	D3S651	18	8	1	Lung	CR 52:873
Unknown	D3S651	8	1	0.25	Breast	CR 53:3804
24-25	RAF1	4		0.33	Cervix	CR 49:3598
24-25	RAF1	3	1 10	1	HeadsNeck	CGC 54:91
25	RAFI	10		0	Kidney	CR 51:4707
25	RAF1	1	0	0.91	Kidney	CR 51:1071
25	RAF1	22	20	0.75	Kidney	CR 51:1544
25	RAF1	12	9 2	0.73 1	Kidney	CR 51:1071
25	RAF1	2	\$0.000 \$0	0.45	Kidney	G 11:537
25	RAF1	22	10	0.43	Kidney	CR 49:1390
24-25	RAFL	17	9	AM-446-4-4-4-4-4-4-4-4-4-4-4-4-4-4-4-4-4-	Lung	GCC 1:95
24-25	RAF1	4	2	0.5	Lung	GCC 1:95
24-25	RAFI	15	14	0.93	Lung	CR 49:5130
25	RAF1	1	1	1	CONTRACTOR OF STREET,	GCC 1:95
24-25	RAFI	1	0	0	Lung	0 4:451
25	RAF1	5	5	1	Lung	G 11:530
25	RAE1	12	2	0.17	Prostate	CR 51:5632
25	RAF1	1	1	1	Uterus	IUC 69:1
24:2-25	D3S1286	37	12	0.32	Esophageal	BJC 73:366
Unknown	D3S1293	33	5	0.15	Esophageal	CR 54:4756
Unknown	D381293	40	2	0.05	<u>HeadsNeck</u>	CR 54:4756
Unknown	D3S1293	39	10	0.26	Head&Neck	CR 52:873
Unknown	D3S1020	5	. 5	1	Lung	A CONTRACTOR OF THE PROPERTY O
Unknown	D3S1020	7	3	0.43	Lung	CR 52:873
Unknown	D391002	5	5	1	Lung	CR 52:873
Unknown	D3S1002	12	3	0.25	Lung	
25.1	D38669	22	3	0.14	Breast	CR 51:5794
25.1	D3S669	10	7	0.7	Kidney	CR 51:4707
Unknown	D3S669	5	5	1	Lung	CR 52:873
Unknown	D35669	12	2	0.17	Lung	CR 52:873

Chromosome 3 - p Arm

Unknown	THRB	54	15	0.28	Breast	GCC_17:128
21-PTER	THRE	30	4	0.13	Breast	AJP 140:215
22-24.1	THRB	71	32	0.45	Breast	CR 54:3021
Unknown	THRB	24	9	0.38	Cervix	IJC 58:787
22-24.1	THRE	7	3	0:43	Cervix.	CR 49:3598
24	THRB	9	1	0.11	Colon	IJC 53:382
24	THRB	44	10	0.23	<u>Esophageal</u>	BJC 73:366
24	THRB	9	3	0.33	Head&Neck	C 72:881
22-24.1	THRB	23.	6	. 0:26	Head4Neck	CR 54:1152
22-24.1	THRB	3	0	0	Head&Neck	CGC 54:91
22-24.1	THRB	. 5	5	1	Kidney	CR 51:949
24	THRB	34	18	0.53	Kidney	G 11:537
22-24.1	THRB	11	11	1	Lung	CR 49:5130
21-PTER	THRB	1	0	0	Lung	GCC 1:95
24	THRB	7	3	0.43	Lung	GCC 3:358
22-24.1	THRB	2	2	1	Lung	GCC 1:95
~22-24.1	THRB	3	i	0.33	Lung	GCC 1:95
22-24.1	THRB	5	3	0.6	Lung	GCC 1:95
. 24	THRB	- 6	'5	0.83	Lung	0 4:451
22-24.1	THRB	10	2	0.2	Lung	GCC 11:15
22-24.1	THRB	72	17	0.77	Lung	GCC 1:95
Unknown	THRB	38	22	0.58	Melanoma	GCC 15:102
24	THRB	22	5	0.23	Owary.	IJC 52:575
22-24.1	THRB	7	4	0.57	Ovary	0 5:219
Unknown	THRB	Z2	- 6	0.27	Ovary	IJC 54:546 BJC 69:429
22-24.1	THRB	17	5	0.29	Ovary	GR 50:3279
Unknown	THRB	16	0	0	<u>Pediatric</u>	GCC 11:119
24	THRB	11	0	0	Prostate	CR 51:5632
Unknown	THRB	2.	0	0	Oterus	CR 51:5632
24	THRB	4	1	0.25	Uterus	G 11:537
24	RARB	5	3	0.6	Kidney	IJC 69:1
24.2-25	D351266	52	15	0.29	Esophageal	CR 51:5794
23	D39647	24	2	0.08	Breast	CR 54:6484
23	D35647	21	8	0.38	Esophageal	BJC 73:36
23	D3S647	30	. 4	0.13	Esophageal	BJC 69:23
23	D3S647	22	8	0.36	Kidney	CR 51:470
23	D3S647	11	5	0,45	Kidney	HG 89:445
pter-21	D3S12	5	0	0	Stomach	IJC 69:1
22-24.2	D381211	17	4	0.24	Emophageal	CR 54:648
21.3	D3S1029	23	4	0.17	Esophageal	JAMA 273:
21.3	D3S1029	1	1	1	Lung	JAMA 273:
21.3	D351029	6	5	0.83	Lung	CR 52:87
Unknown	D3S867	18	5	0.28	Lung	CR 52:873
Unknown	D3S867	7	7	1	Lung	CR 56:197
Onknown	D3S1298	24	8	0.33	Cervix	CR 51:579
13	D3S685	54	б	0.11	Breast	CW 21.212

Chromosome 3 - p Arm

Unknown	039685	6	3		Cervix	GCC_9;119;
21.3-22	D3S1007	17	9	0.53	Esophageal	CR 54:6484
21.3-22	D3S1007	33	6	0.18	Esophageal	BJC_73:366
Unknown	D3S685	47	15	0.32	Esophageal	GCC 10:177
21.3-22	D3S1007	-3	0	0	Kidney-	GCC:12:76
Unknown	D3S685	27	18	0.67	Kidney	CR 51:4707
21.3-22	D3S1007	50	37	0.74	Lung	TJC_64%371
Unknown	D35685	31	14	0.45	Lung	CR 52:873
Unknown	D35685	10	10.	1	Lung	CR.52.878
13	D3S685	1	1	1	Lung	CR 52:2478
13	D3S685	7	7	1	Lung	CR 52:2478
13	D3S685	3	3	1	Lung	CR 52:2478
13	D39685	26	9	0.35	Laing	CR 52:2478*
13	D3S685	18	3	0.17	Ovary	CR 51:5118
Unknown	D3S685	18	******	0,17	Dvarv	CR 51:5178
Unknown	D3S685	11	2	0.18	Uterus	GCC 9:119
22-24.2	D3S1260	63.	25	0.4	Esophageal .	10C 169 11 2
22-24.2	D3S1260	3	0	0	Melanoma	GCC 15:102
21	D3512	16	0	0	Endocrine	CR 56:599*
*****	D3511	7	4	0.57	Kidney	CR 49:1390
21	D3S2-93	1	1	1	Breast	GCC 7:1910
21	D3S2-33	20	1	0.05	Breast	GCC 2:191
21	D392-53	1	0	0	Breast	PN 84:2372
21	Contract to the second contract to the second	2	0	0	Breast	PN 84:2372
21	D3S2-S3	3	0	0	Breast	PN 84:2372
21	D3S2-93	34	2	0.06	Breast	CR 51:5794
21.3	D35686	22	4	0.18	Cervix	CR 54:4481
21	D3S2	44 16	6	0.38	Cervix	IJC 58:787
Unknown	D3S2	10	9	1	Cervix	CR 49:3598
21	. D3SZ	16	3	0.19	Colon	IJC 53:382
21	D3S2	9	0	0	Colon	N 331:273
21	D3S2	***************************************	0	0	Endocrine	GCC 13:9
Unknown	D3S2	12	8	0.36	Esophageal	CR 54:2996
21	D352	22	1	0.1	Esophageal	
Unknown	D3S2	10	11	0.29	Esophagea	BJC 73:366
21.3	D3S68 6	38	***************************************	0.75	Head&Neck	CGC 54:91
21	D3S2	4	3 6	0.43	Kidney	CR 51:949
21	p352	14	(9:9) (000000000000000000000000000000000000	0	Kidney	CR 51:1544
Unknown	D3S2	2	0	0.78	Kidney	CR 51:107
Unknown	D3S 2	23	18	0.5	Kidney	CGC 32:28
Unknown	D3S2	2	11	0.18	Kidney	PNAS 85:1
Unknown	D352	11	2	0.57	Kidney	G 11:537
21	D3S2	14	8	0.45	Kidney	CR: 51:154
Unknown	D3S2	20	9	The second secon	Kidney	CR 49:139
14-21	D3S2	8	7	0.88	Kidney	N 327:721
21	0352	8		0:08		CR 51:470
21.3	D3S686	10	6	0.6	Kidney	CW 211410

Chromosome 3 - p Arm

Unknown	D352	4	1	0.25	Leukemia	CGC 61 (42
21	D3S2	15	12	0.8	Lung	PNAS 84:925
21	D3S2	1	Ó		Lung	PNAS*843925
5000-0000-0000-0000-000-000-000-000-000	D352	5	1	0.2	Lung	GCC 11:15
21	**************************************	5	2	0.4	Lung	GCC 1:95a
21	<u> </u>	************	300 C 3 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1	0	Lung	N 329:451
Unknown	D3S2	1	0		and and the second sec	PNAS. 842925
21	D392-%: -		0	0	Lung	***************************************
21	D3S2	7	7	1	Lung	PNAS 84:925
21	D352	<u>. 8 </u>	6	0:75		PNAS 86-509
Unknown	D3\$2	9	8	0.89	Lung	N 329:451
Unknown	D3S2	1	0,	0	Lung	N 329:453
21	D3S2	6	6	1	Lung	GCC 1:240
21	0352	6	5	0.83%	Lung	PNAS0843925
Unknown	D3S2	20	8	0.4	Lung	JJCR 80:924
Unknown	D392	- 6	5	0,83	Lung	NEUGILL 110
Unknown	D3S2	4	3	0.75	Lung	NEJ 317:110
Unknown	D357	,	1	0.5	Lung-	NEO STREET
Unknown	D3S2	12	0	0	Luna	PNAS 84:925
21	D352	9	4	0.44	Lung	PNAS 867509
***************************************	D352	12	8	0.67	Lung	JJCR 80:924
21			1	0.33	Lung	GCC 1:95
21	D352	3		0.73	Lung	GCC 1:95
21	D3S2	11	8	0.73	Lung	CR 49:5130
21	D3S2	8	8		***************************************	GCC 5:119
14-21	D3S2	5	5	1	Lung	CR: 52:873
21.3	D39686	6	6	1	Lung	CR 52:873
21.3	D3\$686	11	7	0.64	Lung	
Unkanown	D3S2	11	- 6	0.55	<u>Melanoma</u>	GCC 15:102
Unknown	D3S2	6	0	0	Neuroblas	com CR 49:1095
		***************************************			a	IJC 54:546
21	D3S2	1.6	1	0.06	Ovary	***************************************
21	D352	6	4	0.67	Sarcoma	CGC 53:45 CR 52:2419
21	D352	12	4	0:33	Sarcoma	WAY THE SECTION AND ASSESSMENT OF THE SECTION ASSESSMENT OF THE SECTIO
Unknown	D352	10	0	0	Stomach	CR 48:2988
Unknown	D3S2	19	1	0,05	Testis	0 9:2245
21	D3S2	12	4	0.33	Testis	G 5:134
Unknown	D352.	5	0	G	Dterus	CR 51:5632
14.2	D3S3	1	0	0	Breast	GCC 2:191
14.2	D393	9	9	1	Head&Neck	CGC 54:91
14.2	D3S3	4	3	0.75	Kidney	CR 51:1071
142	0353	1	1	1	Kidney	CR 49:1390
Company and Commence and Commen	D3S3	9	0	0	Kidney	PNAS 85:157
14.2	D3S3	2	1	0.5	Kidney	N 327:721
14:2	**************************************	**************************************	***************************************	0.33	Kidnev	G 11:537
14.2	D3S3	3	1	0.6	Lung	GCC 1:95
14.2	D3S3	5	~,>>>>	***************************************	Lung	GCC 1:95
14.2	D3S3	1	1	1	THE RESERVE THE PARTY AND PARTY AND PARTY.	GCC 1:240
14.2	p3s3	4	4	<u> </u>	Lung:	N 329:451
14.2	D3S3	1	0	0	Lung	N 323.431

PCT/US98/05419

Chromosome 3 - p Arm

14.2	_D3S3	9	6	0.67	Lung	N:329:451
14.2	D3S3	3	3	1	Lung	GCC 1:95
14.2	D393.	ì	0	- 1 - 0 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1	Lung	N3329:4515
14.2	D3S3	2	1	0.5	Lung	NEJ 317:110
1472	10383	4		0.015	anna sa	STATE OF STATE
14.2	D353	4	0	0	Lung	GCC 11:15
14.2	C280	100	1		James Land	71666451805
21.2-14.2	D3S32	8	0	0	Brain	CR 49:6572
21.2-14:2	75832	18	2		Biraili	CRL50:5784
21.2-14.2	D3\$32	16	3	0.19	Breast	CR 50:7184
21:2-14.2	D3832	44	9	0.2	Breast	FR 451-45794
21.2-14.2	D3S32	30	12	0.4	Cervix	CR 54:4481
14.2-21.2	03532	4			Cervix	*GCC 3:119:
21.2-14.2	D3S32 .	17	7	0.41	Cervix	IJC 58:787
34 (2=212	03837	4		39,0225	Cervix	.BJC167:71
14.2-21.2	D3S32	19	8	0.42	Esophageal	CR 54:2996
2172-14.2	03\$32	- 28	10	0.36	Esophageal	BJC 73 366
21.2-14.2	D3S32	7	0	0	Head&Neck	C 72:881
71.2-14.7	03837	15	8	- 0.53	Kidney	CR_51:820 ~
14.2-21.2	D3S32	15	9	0.6	Kidney	CR 51:4707
14.2-21.2	D3S32	21	17	0.81	Kidney	CR-51:1071
21.2-14.2	D3S32	18	8	0.44	Kidney	CR 51:949
21:2-14:2	D3932	20	7	0.1	Liver	CR 51:89
21.2-14.2	D3\$32	11	6	0.55	Lung	GCC 3:358
21.2-14.2	D3S32	17	11	0.65	Lung	CR 57:873
21.2-14.2	D3S32	6	6	1	Lung	0 4:451
21.2-14.2	D3532	5	1	0.2	Lung .	GCC 11:15
21.2-14.2	D3S32	4	4	1	Lung	CR 52:873
21.2-14.2	D3S32	17	10	0.59	Melanoma	GCC 15:102
21.2-14.2	D3S32	13	2	0.15	Ovary	IJC 54:546 CR 51:5118
21,2-14,2	D3532	17	3.	0.18	Ovary	CR 51:5118
21.2-14.2	D3S32	17	3	0.18	Ovary	CR 54:2761
21.2-14.2	D3S32	3	11	0.33	Pancreas	PNAS 87:875
21.2-14.2	D3S32	10	1	0.1	Prostate	CSurveys 11
21,2-14.2	D3532	10	1	0.1	Prostate	O 9:2245
21.2-14.2	D3S32	33	15	0.45	Testis	GCC 9:119
21.2-14.2	D3S32	4	2	0.5	Oterua	GCC 15:102
21.2-21.1	D3S1289	15	5	0.33	Melanoma	CR 51:5794
21,32-21.33	D3S643	14	4	0,29	Breast	CR 54:6484
21.32-21.33	D3S643	19	0	0	Esophageal Kidney	CR: 51: 4707
21.32-21.33	D3S643	3		0.24	Leukemia	B 83:3449
21.32-21.33	D3S643	17	4	0.24 0.5	Lung	CR 52:873
21.32-21.33	D3S643	5	3	<u> </u>	Lung	CR 52:873
21.32-21.33	D3S643	3 15	3 7	0.47	Breast	GE: 5:554
<u>21</u>	D3E1592	***************************************	5	***************************************	Breast	CR 53:4356
21	D3F15S2	33	5	0.15	DIEGZE	C# 33.4330

Chromosome 3 - p Arm

				0	Cervia	CR 49:3598
21	D3F15S2	2	0	0.6	Cervix	IJC 59:787
21	D3F15S2	5	3		Esophageal.	EJC 308,748
71	D3F15S2	21		0.75	Head&Neck	C 72:881
21	D3F15S2	12	9		Head&Neck	CGC 54:91
21	D3F1592)	7	. 2		Kidney	CGC 32:281
	D3F15S2	3	3	1	Kidney	
21	D3F1582	3	0	, 2 0 ±	Kidney	G 11:537
71	D3F1552	24	14	0.58	Kidney	
21	D3F1592	7	1	. 0.14		CR 49:1390
21	D3F15S2	13	10	0.77	Kidney	PNAS 85:157
21	D3F1552	21	16	0.76	Kidney	N 327:721
71	D3F15S2	9	9	1	Kidney	CR 51:949
21		2.		. 0.5	Kidney	
21	D3F1592	16	12	0.75	Kidney	N_3297451
21	D3F15S2	10	1	. 0	Lung	N 329:451
21	03F1552	9	9	1	Lung	GCC 119156
21	D3F15S2	7	3	0.43	Lung	N 329:451
21:	D3F1592	1	0	0	Lung	CL 51:133
21	D3F15S2	7	2	0.29	Lung	
21	D3F15S2	8	3	0.38	Lung	PNAS 86:509 GCC,3:358
21	D3F1552	8	2	0.25	Lung	
21	D3F1592		3	0.5	Lung	PNAS 86:50
21	D3F15S2	6	0	0	Lung	PNAS 86:50
21	D3F15S2	2	0	0	Lung	CL 51:133
21	D3F15S2	2	4	0.8	Lung	0 4:451
21	D3F1592	5	0	0	Lung	GCC 1:95
21	D3F15S2	1	3	0.6	Lung	NEJ, 317:17
21	D3F1582	5	***************************************	0.57	Lung	GCC 1:95
21	D3F15S2	7	- 4	O	Lung	GCC 1:95
21	D3F1592	1		1	Lung	CR 49:513
21	D3F15S2	2	2	0.69	Lung	GCC 1:95
21	D3F15S2	16	11	0.58	Melanoma	GCC 15:10
21	D3F15S2	12	7	0.12	Ovary	0 5:219
21	D3F1592	8:	1	0.18	Ovary	IJC 52:57
21	D3F15S2	22	4	0.18	Ovarv	TJC 54:58
21	D3F15\$2	22	4	0.17	Ovarv	BJC 69:42
21	D3F15S2	12	2	0.17		CCG 52:7
21	D3E1592	3	0	0	Testis	CCG 52:7
21	D3F15S2	1	0	0	Testis	CCG 52:7
21	D3F15S2	2	0	deterior de la companya del la companya de la compa	Testis	GCC 13:2
::-	D3F15S2	18	2	0.11	Dterus	CR 51:56
21	D3F15S2	2	0	0	Esophage	al BJC 73:3
21	D3S1076	29	2	0.07	Esophagi	ER 54:64
Unknown	0351076	1.4	4	0.29	Kidney	BJC 69:2
Unknown	D351076	22	13	0.59		CR 52:8
Unknown	D381076	4	0	0	Lung	CR 52:8
Unknown		TO SOURCE SERVICE SERV	1	1	Lung	

Chromosome 3 - p Arm

		33	6	0.18	Breast	CR 51:5794
21.2	D35660.	6	2	0.33	Kidney	CR 51:4707
Jnknown	D3S660	0	2	0.742	Lung	CR: 52:1978
Jnknown	*D35660 ****	8	В	1	Lung	CR 52:873
Jnknown	D3S660	6.	0	0.5	Keidhes	CR:51:4707
Unknown : :	pacy) 77		2	0.5	Lung	CR 52:873
Unknown	D3S717	4	2		remer	GR 52:873
Unknown	D3S717	***	4	0.36	Kidney	CR 51:4708
Unknown	D3S936	11		0.42	Lime	, CR-57:673
Unknown	D35936		4	1	Lung	CR 52:873
Unknown	D35936	4	**	0.2	Esophageal	
4.2-21.1	0391313	54	19	0.36	Esophageal	IJC 69:1
4.2-21.1	D3S1300	53 50	19	0138	Breast	CR 51:5794
4,2-14,3-	D39628	10	7	0.7	Kidney	CR 51:4707
14.2-14.3	D35678			0_32	Breast	CRI 51/5/94
Unknown	- D3858/Jul	13	8	0.62	Kidney	CR 51:4707
Unknown	D3S687	13			10000	GR 57-870
Onknown:	D39687.22.2	15	3	0.2	Lung	CR 52:873
Unknown	D3S687	37	3	0.13	Esophageal	BJC(73: 366
Unknown	D381228		8	0.44	Esophageal	CR 54:6484
25	D3S1228	18	12	0.46	Kidney	BJC 69:230
25	D3S1228	26	4	0.67	Lung	JAMA 273:5
25	D3S1228	6	1	1	Lung	JAMA 2731
25	D391228	<u>1</u> 47	18	0.38	Esophageal	IJC 69:1
14.1-14.2	D351285	10	10	0.7	Melanoma,	GCC 15:10
14.1-14.2	D3S1285	24	1	0.04	Breast	CR 51:579
Unknown	D3S714	24 9 -	3.	0.33	Lung	CR 52:873
Unknown	D3S714:	****	18	0.64	Esophagea	C 73:2472
14-13	D3S1217	28	18	0.64	Head&Neck	CA 73:247
14-13	D351217	28 25	4	0.16	Esophagea	1 BJC 73:36
Unknown	D3S1079		4	0.36	Esophagea	1 CR 54:64
Unknown	0391079	11 20	8	0.4	Cervix	CR 56:19
Unknown	D3S1261	20	Ö	0	Stomach	AG 89:44!
Unknown	D3S13		17	0.3	Esophagea	l IJC 69:1
12-14.2	D3S1296		23	0.43	Breast	CR 51:57
Unknown	D3S659	54	6	0.86	Cervix	GCC 9:11
Unknown	D3S659	7	10	0.36	Esophage	1 GCC 10:1
Unknown	D3S659	28	6	0.17	Esophage	al BJC 73:3
Unknown	D35659	36	7	0.41	Esophage	1 CR 54:64
Unknown	D3\$659	17	8	0.73	Kidney	CR 51:47
Unknown	D3S659	11	18	0.45	<u>Kidney</u>	BJC ,69:2
Unknown	D38659	40	- 10	0.29	Lung	CR 52:87
Unknown	D3S659	17	9	0.9	Lung	CR 52:8
Unknown	D35659	10	0	0	Ovary	CR 51:5
Unknown	D3S659	6	0	0	QASTA	CR 51(5
Unknown	035659	6		0.45	Uterus	GCC 9:1

Chromosome 3 - p Arm

	D3S659	14	1	0.07	Uterus	CR 54:4294
Unknown		6	0	0	Breast	CR 51:5794
13	D3S693	1		0.	*Lung	CR+52:8135
13		32	11	0.34	Breast	CR 54:499
14	D3S6	5	The state of the s	0.4	ekaraney	CR#49:1390
14	D386%	3	0	0	Kidney	PNAS 85:157
14	D3S6	3		10-33	Kidney	Completely and
. 14	D396) .		7	0.88	Lung	GCC 1:95
14	D3S6	8	2	0.33	Lung	GCC 1:95 #
. 14	.D366	6	2	0.5	Lung	GCC 11:15
14	D3S6	4	55	0.83	Lung	10(e46(=192)
21.3	ITIH12H3.	66		0.41	Breast	CR 54:3021
Unknown	D3S30	37	15		Breast	CR448-1608-
13	09550	18	0	0.35	Cervix	IJC 58:787
Unknown	D3S30	17	6		Esophageal,	water and the second of the second of
Unknown.	AND SECURITY OF SECURITY SECUR	19	. 6		Esophageal	BJC 73:366
13	D3S30	32	12	0.38 0.5		GREEN VERVE
(Takaom	er en op stad op een de	16		***	Kidnev	CR 51:820
13	D3S30	18	9	0.5	Lung	CR 52:873
Unknown	.02820	12.	3	0.25	Lung	GCC 11:15
13	D3S30	7	1	0.14		CR 52 873
Unknown	D3S30	11	11	1	Lung -	GCC 1:240
13	D3S30	7	7	1	Lung	GCC 15:102
Unknown	D3530	11	8	0.73	Melanoma	CR 51:5118
13	D3S30	14	1	0.07	Ovary	CR 51;5118
13	D3S30	14	1	0.07	OVERY	BJC 69:429
Unknown	D3530	12	1	0.08	Ovary	G 5:134
13	D3530	18	-0	0	Testis	CR 54:1152
13-14	D3S1284	19	12	0.63	Head&Neck	GCC 12:76
13-14	D3S1284	3	0	0	Kidney	GCC 5:119
Unknown	D3S738	3	3	1	Lung	GCC 5:119
Unknown	D3S625	2	7	1	Lung	GCC 5:119
Unknown	D35742	4	3	0.75	Lung	GCC 5:119
Unknown	D35739	- 5	3	0.6	Lung	GCC 5:119
	D3S740	5	4	0.8	Lung	
Unknown	D3S216	1	1"	1	Lung	GCC 5:119
Unknown	D3S733	3	3	1	Lung	GCC 5:119
Unknown	D35733	16		0.44	Kidney	CR 51:949
13	D3S4	17	4	0.24	Kidney	CR 51:107
13	D3S4	14	8	0.57	Kidney	CR 49:139
13	***************************************	6	5	0.83	Lung	GCC 1:240
13	D3S4	5	4	0.8	Lung	GCC 57219
Unknown	D35743	7	6	0.86	Lung	GCC 5:119
Unknown	D35759	5	3	0.6	Lung	GCC 5:119
Unknown	D3S640		2	1	Lung	GCC 5:119
Unknown	D351090	2 2		1	Lung	GCC 5:119
Unknown	D3S1090	Sec. 15 1. 1888.	a versa karantari katalogia (Karantari Karantari Karantari Karantari Karantari Karantari Karantari Karantari K	The state of the s		CR 55:521

Chromosome 3 - p Arm

	TARE DISTERS	25	12	0.48	Bladder	CR 51:5405
Unknown	RAFI-DNF15S2 Unknown	28	13	0.46	Breast	JNCI 84:506
24-26	D392-H3H2	37	12	0.32	Breast	CR 54:3021
Unknown	DNF15S2	4	1	0.25	Breast	CR 53:3804
Unknown	EABMD.	67	76	0.39	Breast	CR_541499
24	RAF1-DNF15S2	15	7	0.47	Breast	GE 5:554
Unknown	The second secon	6		0.5.	CHIVEX	* GCC, 9:119
Unknown	D3S663	20	7	0.35	Esophageal	CR 54:6484
21.1-14.2	D3S1067	17	7	0.41	Esophageal	CR 54:6484
Unknown	D3S1110	11	1	0.09	Esophageal	CR 54:6484
Unknown	D3S1111	34	8	0.24	Esophageal	BJC 13:366
Unknown,	D3S192	19	8	0.42	Esophageal	CR 54:6484
Unknown	D3S656	22"	2	0.09	Esophageal	CR 54:6484
Unknown	D3S663		. 0	0.24	Esophageal	BJC 73:366
Unknown	D3S966	38 19			Esophageal	CR 54:6484
- Undenova	D3S966		20	0.49	Kidney	BJC 69:230
21.1-14.2	D3S1067	41	3		Kidney	CR-51_4707
25-25	0351085		11	0.73	Kidney	BJC 69:230
Unknown	D3S1110	15		0.41	Kidney	PNAS 92:28
Unknown	D391263-D391307-	- 22	9	V-74		
	D3S1297	- 6	0	0	Kidney	PNAS 92:285
Unknown	D3S1263-D3S1307- D3S1297	- 0	Ů			
	D3S22	j.	7	0.78	Kidney	CR_51:1071
Unknown	D35449	11	7	0.64	Kidney	CR 51:4707
25	D3S654	13	4	0.31	Kidney	CR 51:4707
Unknown		7	4	0.57	Kidney	CR 51:4707
Unknown	D3S656	i	. 0	G.	Kidney	CR*51:4707
25		11	5	0.45	Kidney	CR 51:4707
25-26	D3S858	8	7	0.88	Kidney	CR 51:470
Z1.1-21.2	D3S898	6	2	0.33	Kidney	CR 51:470
14.1-14.2	D3S907	2	2		Kidney	CR_51;470
12	D35960	***************************************	10	0.3	Kidney	CR 55:618
Unknown	D3S:1263-1307- 1297	. 33	10			
	DNF1592	28	25	0.89	Kidney	CR 51:107
Unknown	DNF1532	19	9	0.47	Kidney	CR 51:154
Unknown	ERBA-B	18	17	0.94	Kidney	CR 51:107
Unknown	ERBA-B	2	0	0	Kidney	CR 51:107
Unknown		MS 600 00000 A 10000 CONT.	7	0.54	Kidney	CR 51:949
Unknown	RAF1-DNF15S2	19	16	0.84	Kidney	CR 54:285
25-26	VHL	Commence of the last of the la	25	0.93	Lung	CR 54:232
Unknown		27	11	0.92	Lung	IJC 64:37
21.3	D3S1339	12	5	1	Lung	GCC .5:115
21	D3S48	5	7	0.78	Lung	CR 52:87
Unknown	D3S654	9	8	0.36	The second secon	CR 52:87
Unknown	V-V-V-V-V-V-V-V-V-V-V-V-V-V-V-V-V-V-V-	22		0.2	Lung	NEJ 317:
Unknown	DNF15S2	5	1	0.2	Lung	NEJ 317:
Unknown	DNE1592			1	Lung	NEJ 317:
Unknown	DNF15S2	5	5	1		

Chromosome 3 - p Arm

lnknown	ITIH1-D39:1339-			•	Lung	37.1.2
Jnknown	RAF1-DNF15S2	4	4	1	Lung	GCC 5:119
Покломп	RAFI-DWE15S2	6	7 (V)	0.5	Lung	PNAS B6:
Jnknown	RAF1-DNF15S2	5	3	0.6	Lung	PNAS 86:5
Unknown	RAFIL-DAF1582	17.	8	0.4	Lung Melanoma	GCC 15:10
25-24	D3S1252	5	1	0.2 0.24	Ovary	CR 53:44
all	7 loc1#	46	- 11	0.24	Ovarv	CR 53:23
21	D3S2-D3S86	23	0	0.14	Ovary	BJC 72:1
Unknown	D39:1270-11	1.0	2	0.11	Testis	G 5:134
Unknown	Unknown D3S1067	25	-	0.12	Oterus	CR.54:42
1,1-14.2	D3S1063	23 10	2	0.2	Üterus	GCC 9:11
Unknown SOM	03963	- 5933	2353	0:4		

Chromosome 3 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Refere
11.0-12.0	GPX1	19	17	0.89	Kidney	.Cr.15
11.0-12.0	GPX1	6	6	1	Lung	Cr 15
11.0-12.0	GPX1			1	Lung	Cr 15
12	D3S1	7	0	0	Head&Neck	CGC 5
12	D951	12.09	0.0	0	Kidney	CGC63
12	D3S1	4	С	0	Lung	NEJ 3
12	D3S1	4	- 0	0	Lung	0.414
12	D3S1	1	0	0	Lung	N 329
12	D351	9	2	0.22	Lung	N/329
12	D3S1	1	0	0	Lung	N 329
12	D3S1.	10	7	0.11	Ovary	-1003
12	D3S1	8	1	0.12	Testis	GCC 1
Unknown	D3S1764	~ * * * 7.4	-	0.04	Esophageal	************
Unknown	D3S196	31	3	0.1	Esophageal	BJC 7
Unknown	D33190	19		0.47	ReadsNeck	
Unknown	D3S196	19	5	0.26	Ovary	BJC 6
Unknown	D38196°°°	22	2	0:09	Uterus	CR 54
Unknown	CP		1	0.14	Lung	N 329
CONTRACTOR AND AND ASSESSMENT ASS		1		0.14	***************************************	
Unknown	CP	***************************************		······································	Lung	<u>"N 329</u>
Unknown	CP	1	0	0	Lung	N 329
Unknown	D3S1268	24	2	0.08	Head&Neck	CR:54
Unknown	D351268	34	0	0	Head&Neck	CR 54
Unknown	D391268	35	5.	0.14	<u> Melanoma</u>	CR 5
Unknown	D3S1262	37	8	0.22	Cervix	CR 56
Unknown	D3S1262	18	1	0.06	Esophageal	CR 54
28	SST	6	0	0	Cervix	CR 49
28	SST	6	- 0	0	Liver	CCG
28	SST	9	2	0.22	Lung	N 32
28	SST	12	0	0	Long	PNAS
28	SST	1	0	0	Lung	N 32
28	SST	7	0	0	Lung	CR 4
28	SST	1	0	0	Melanoma	N 32
28	SST	3	0	0	Neuroblast	m CR 4
					a	
Unknown	D3S1314	26	1	0.04	Kidney	PNAS
Unknown	D3\$42	4	.1	0.25	Breast	CR 5
Unknown	D3S42	26	3	0.12	Breast	GCC
Unknown	D3542	28	9	0.32	Cervix	CR.5
Unknown	D3542	12	0	0	Stomach	HG 9
Unknown	D3S42	34 .	9	0.26	Testis	0 9:
Unknown	D3S42	16	0	0	Testis	LI 7
Unknown	D3542	35	6	0.17	Overv	CR 5
Unknown	D3546	19	5	0.26	Esophageal	CR 5
AND THE PROPERTY OF THE PROPER		19	3	0.26	Esophageal	1000 Carried Way
Unknown	D3S46	***************************************			·····	GCC
Unknown	D3S46	4.4	13	0.3	Esophageal	600

Chromosome 3 - q Arm

44 / 214

Unknown	D3S46	7	0	0	Liver	CR 51
Unknown 🤾	D3S46	20.0	6	0.35	Jung .	Secretary CPX
Unknown	D3S46	18	1	0.06	Ovary	CR 51
Unknown	20 (0459) et al.	10		0.00	Over-	# 15 (C T M
Unknown	D3S46	3	0	0	Pancreas	CR 54
Unknower i	2277 PK 67 (* 2744.51)	and have	ters of Europe	10.0F	Sarcona	6.000
Unknown	D3S46	12	9	0.75	Sarcoma	CR 52
Unknown -	Onknown	16	0.00	0	Brath .	10.4.10
21-qter	D3S5	1	0	0	Brain	CCG 5
Unknown	MOX2			0.00	10.710	Section S
Unknown	D3S47	21	0	0	Endocrine	GCC 1
Unknown	GRIEV2	23				• • • • • • • • • • • • • • • • • • •
Unknown	D3S1271	14	1	0.07	Esophageal	CR 54
Unknown :	035,238	P10			THE PROPERTY.	
Unknown	D3S1-MOX2-D3S5	24	2	0.08	Kidney	G 11:
Unknown »	p3931			- x = (0 2 40	#Krideva	
26.2-qTER	D3S45	20	3	0.15	Kidney	CR 51
Alla	4.markers:	32 -	7.6	0.40	Ilung	*** (• •) *
12-q13	MOX1	15	7	0.47	Lung	GCC 1
12:913	MOX1	6	2	0.33	Long	GCC 1
12-q13	MOX1	1	1	1	Lung	GCC 1
12-q13	, MOX1	1	1.	1	Lung	GCC_1
all	4 markers	46	8	0.17	Ovary	CR 53
21-PTER	ACCP	13	. 4	0.31	Overy	BJC:6
Unknown	D3S1232-GLUT2	14	2	0.14	Ovary	BJC 7
Unknown	: D3S31	13	0	0	Prostate	G.111
SUM		1050	191	0.18		

Chromosome 4 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
16.1	RAF1P1	7	0	0	Uterus	CR 51:5632
Unknown	D4S1546	25	8	0.32	Bladder	CR 55:5213
Onknown	D45124	16	0	. 0	Brain	CR 50:5784
16	D4S10	31	0	0	Breast	GE 5:554
pter-16.3	D4S125	6	1	0.17	Breast	CR 50:7184
16	D4S95	33	4	0.12	Breast	CR 53:4356
pter-16.3	D4S125	9	0	. 0	Cervix	CR 54;4481
Unknown	D4S125	2	0	0	Cervix	GCC 9:119
Unknown	D4S391	25	9	0.36	Cervix	CR 56:197
Unknown	D4S405	30	4	0.13	Cervix	CR 56:197
16	D4S10	11	0	0	Colon	CCG 48:167
pter-16.3	D4S125	8	0	0	Colon	CCG 48:167
11.0-15	D4S174	21	0	G	Endocrine	GCC 13:9
Unknown	D4S2397	18	1	0.06	Endocrine	CR 56:599
Unknown	D45124	21	2	0.1	Esophageal	CR 54:2996
Unknown	D4S125	40	7	0.17	Esophageal	GCC 10:177
pter-16.3	D4S125	9	O	0	Esophageal	CR 51:2113
Unknown	D4S394	15	1	0.07	Head&Neck	CR 54:4756
Unknown	D45394	18	. 0	0	Head&Neck	CR 54:4756
Unknown	D4S404	21	8	0.38	Head&Neck	CR 54:1152
pter-16.3	D4S125	7	0	0	Kidney	CR 51:820
Unknown	D4S431	28	2	0.07	Kidney	PNAS 92:2854
16.3	D4S10	. 5	1	0,2	Liver	CCG 48:72
16	D4S10	6	2	0.33	Liver	CR 51:4367
pter-16.3	D4\$125	4	0	. 0	Liver	CR 51:89
Unknown	D4S125	6	0	0	Liver	PNAS 86:8852
16.1	RAF1P1	13	2	0.15	Liver	JJCR-81:108
pter-16.3	D4S125	28	2	0.07	Lung	CR 52:2478
pter-16.3	D4S125	24	10	0.42	Ovary	CR 51:5118
Unknown	D4S125-D4S124	29	10	0.34	Ovary	CR 53:2393
, :15:1-11. ;	D4S16	19	2	0.11	Ovary	IJC 54:546
11.0-15	D4S174	20	3	0.15	Ovary	BJC 69:429
16,2-15,1	D4S49	20	,5	0.25	Ovary	IJC 54:546
12.0-13	GABRB1	16	2	0.12	Ovary	BJC 69:429
pter-16.3	D45125	3	Ö	C	Pancreas	CR 54:2751
12.0-13	GABRB1	13	0	0	Prostate	G 11:530
Unknown	D4S124	13	1	0.08	Sarcoma	CR 52:2419
Unknown	D45125	17	3	0.18	Testis	0 9:2245
pter-16.3	D45125	. 9	0	0	Testia	li 73:606
Unknown	D4S129	10	1	0.1	Testis	GCC 13:249
pter-16.3	D4S125	2	O.	0	Uterus	GCC 9:119
11.0-15	D4S174	21	1	0.05	Uterus	CR 54:4294
16	D4543	25	1	0.04	.Oterus	CR 54:4294
12.0-13	GABRB1	25	0	0	Uterus	CR 54:4294
16.1	RAF1P1		0	0	Uterus	CR 51:5632

WO 98/41648

46 / 214

PCT/US98/05419

Chromosome 4 - p Arm

SUM

729

93 0.13

Chromosome 4 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
p11-g21	MT2P1	4	0	0	Dterus	CR 51:5632
33-35	D4S171	29	15	0.52	Bladder	CR 55:5213
25-34	D49243	29	15	0.52	Bladder	CR 55:5213
Unknown	Unknown	20	2	0.1	Brain	CR 50:5784
Unknown	D4S125	34	. 2	0.06	Breagt	CR 50:7184
25-34	D4S192	54	13	0.24	Breast	BCRT 32:5
28	FGA	19		0.21	Breast	GCC 2:191
28	FGA	18	C	0	Breast	CR 53:4356
p11-q21	MT2P1	17	0	Ö	· Breast	JNCI 84:506
21-23	ADH3	22	12	0.55	Cervix	CR 54:4481
21-25	ADH5	24	11	0.46	Cervix	CR 54:4481
Unknown	D4S163	41	12	0.29	Cervix	CR 54:4481
Unknown	D45103	28	12	0.29	NO. ACCRECATE VALUE OF THE PARTY OF THE PART	TO COMPANY AND DESCRIPTION OF THE PARTY OF T
Unknown	D4S415	26	8	0.23	Cervix	CR 56:197
gl1=gl3	ALB	******************		PROPERTY NAMED AND ADDRESS OF THE PARTY AND AD	Cervix	CR 56:197
***************************************	***************************************	11	0	0	Colon	CCG 48:167
Unknown	D4S415	19	1	0.05	Endocrine	CR 56:599
Unknown	D4S163	. 21	2	0.1	Esophageal	CR 54:2996
Unknown	D4S163	35	9	0.26	Esophageal	GCC 10:177
Onknown	D49402	16	3	0.19	Head&Neck	CR 54:4756
Unknown	D45402	20	1	0.05	Head&Neck	CR 54:4756
Unknown	D4S430	24	9	0.38	Read&Neck_	CR 54:1152
Unknown	D4S163	23	2	0.09	Kidney	CR 51:820
***************************************	D48426-D48415	************	1	0.05	Kidney	PNAS 92:2854
A CONTRACTOR OF THE PROPERTY OF THE	D4S426-D4S415		0	0 .	Kidney	PNAS 92:2854
Unknown	D45:408-429	23	4	0.17	Loukemia	CR 55:5377
Unknown	Unknown	8	0	0	Liver	BJC 64:1083
21-23	ADH3	4	0	<u> </u>	Liver	JJCR 81:108
21-23	ADH3	6	1	0.17	Liver	CR 51:4367
gll-gl3	ALB	5	5	1	Liver	PNAS 8618852
Unknown	D4S16	5	2	0.4	Liver	JJCR 81:108
Onknown	D4S163	20		0.15	Liver	CR 51:89
p11-g21	MT2P1	16	8	0.5	Liver	JJCR 81:108
pl1-q21	MT2Pl	21	9	0.43	Liver	JJCR 84:893
p11-g21	MT2P1	19	4	0.21	Liver	CR 54:281
Unknown	D49163	31	8	0,26	Lung	CR 52:2478
21-23	ADH3	18	1	0.06	Ovary	IJC 54:546
11.0-15	D4S1540	20	3	0.15	Overy	BUC 69:429
11.0-15	D4S1607	20	3	0.15	Ovary	BJC 69:429
Unknown	D49163	16	1	0.06	Ovary	CR 51:5118
33-35	D4S171	12	4	0.33	Ovary	BJC 69:429
25-34	D4S175	20	7	0.35	Ovary	BJC 69:429
Unknown	D4S27	29	10	0.34	Ovary	CR 53:2393
pl1-q21	MT2P1	21	2	0.1	Ovary	IJC 54:546
35	Unknown	6	1	0.17	Pancreas	CR 54:2761
28	FGA	9	0	0	Prostate	G 11:530
Unknown	D4S163	17	3	0.18	Sarcoma	CR 52:2419
		-	_			

Chromosome 4 - q Arm

21-23	EHDA	.24	0	0	Testis	0 9:2245
33-35	D4S171	23	0	0	Uterus	CR 54:4294
p11-q21	MT2P1	4	0	0	Uterus	CR 51:5632
SUM		952	209	0.22		A CONTRACTOR OF THE PROPERTY O

Chromosome 5 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
Unknown	D55392	34	. 8	0.24	Cervix	JNCI 87:742
Unknown	D5S392	19	0	0	Endocrine	CR 56:599
Unknown	059392	26	5	0.19	HeadsNeck	CR 54:1152
Unknown	D5S392	19	0	0	Kidney	PNAS 92:2854
Unknown	D5S392	5	0	0	Kidney	PNAS 92:2854
Unknown	D5S13	21	1	0.05	Breast	CR 53:4356
Unknown	D5S13	17	4	0.24	Breast	GCC 2:191
pter-p15	D5S4	10	1	0.1	Breast	GCC 2:191
pter-p15	D5S4	17	2	0.12	Colon	IJC 53:382
pter-p15	D5S4	11	0	0	Colon	CCG 48:167
pter-pl5	D554	29	i -	0.03	Colon	CR 50:7166
pter-p15	D5S4	19	4	0.21	Ovary	CR 53:2393
pter-p15	D5S4	3	Q.	0	Testis	CCG 52:72
pter-p15	D5S4	1	0	0	Testis	CCG 52:72
pter-p15	D554	1	0	0	Testis	CCG 52:72
15.1-15.2	D5S406	25	12	0.48	Cervix	JNCI 87:742
15.2-15.1	D5S12	12	1	0.08	Brain	CR 50:5784
15.2-15.1	D5S12	13	5	0.38	Cervix	CR 54:4481
15.2-15.1	D5S12	9	0	0	Ovary	0.5:219
15.2-15.1	D5S12	17	0	0	Prostate	G 11:530
15.2-15.1	D5S12	26	11	0.42	Testis	0 9:2245
15.1-15.3	D5S208	20	10	0.5	Cervix	JNCI 87:742
15-21	D55630	5	2	0.4	Lung	0 12:97
15-21	D5S630	13	3	0.23	Lung	0 12:97
14	D5S432	29	8	0.28	Cervix	JNCI 87:742
15.1-15.3	D5S117	25	8	0.32	Cervix	JNCI 87:742
15.1-15.3		13	2	0.15	Ovary	BJC 69:429
15.1-15.3	D5S117	2 2	1	0.05	Uterus	CR 54:4294
Unknown	D5S268	14	3	0.03	Ovary	BJC 69:429
Unknown	D5S419	26	3	0.12	Cervix	CR 56:197
Unknown	059419	28	Q	0.12	Head&Neck	CR 54:4756
Unknown	D5S419	16	3	0.19	Head&Neck	CR 54:4756
14	D5519	23	13	0.57	Cervix	CR 54:4756
Unknown	D5S395	28	6	0.21	Cervix	CR 56:197
13	D5\$20	21		0.05	Ovary	IJC 54:546
11.0-13	D5S21	9	5	0.56	Cervix	CR 54:4481
11.0-13	D5521	THE PARTY OF THE P	5	0.56	Cervix	CR 54:4481
Unknown	Unknown	4	0	0	Brain	CR 49:6572
Unknown	D5S1	5	· · · · · · · · · · · · · · · · · · ·	0.2	Breast	GCC 2:191
Unknown	Unknown	5	0	0	Colon	BJC 67:1007
Unknown	D5S1	3	Ö	Ö	Colon	CCG:48:167
Unknown	D5S1	28	7	0.25	Esophageal	CR 54:2996
Unknown	Unknown	4	Ó	0.23	Kara kara kara janggaran Karamanan kara	BJC 67:1007
Unknown	Unknown	8	3	0.38	Liver Liver	BJC 64:1083
Unknown	Onknown	3	0	0.38		
Unknown	Unknown	7	0	0	Pancreas	CR 54:2761
Oll Allowit	CHALLOWII	,	U	U	Pancreas	BJC 65:809

Chromosome 5 - p Arm

Unknown Unkn	own 29	1	0.03 Te	stisGCC 13:249
SUM	722	135	0.19	

Chromosome 5 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
15-21	D59491	1	0	0	Lung	0 12:97
15-21	D5S491	8	3	0.38	Lung	0 12:97
Unknown	D5S427	22	4	0.18	Cervix	CR 56:197
11.2-13.3	D5S6	30	1	0.03	Breast	GE 5:554
11.2-13.3	D596	. 4	2	0.5	Colon	0 9:991
11.2-13.3	D5S6	32	9	0.28	Colon	CR 50:7166
11.2-13.3	D5S6	17	1	0:06	Pediatric	CR 50:3279
15-21	D5S637	5	1	0.2	Lung	0 12:97
15-21	D59637	9 .	6	0.67	Lung	O 12:97
15-21	D5S626	4	1	0.25	Lung	0 12:97
15-21	D5S626	17	9	0.53	Lung	0 12:97
Unknown	D5S107	19	2	0.11	Leukemia	B 83:3449
Unknown	059107	33	2	0.06	Stomach	CR 56; 612
Unknown	D5S107	30	1	0.03	Uterus	CR 54:4294
Unknown	D5S428	20.	7	0.35	Stomach	CR 56:612
Unknown	D5S37	2	0	0	Colon	0 9:991
Unknown	D5537	11	<u> 6</u>	0.55	Colon	CR 50:7166
Unknown	D5S37	28	7	0.25	Esophageal	CR 54:2996
Unknown	D5937	3	0	0	Liver	CCG 48:72
Unknown Unknown	D5S37	12	5 4	0.42	Sarcoma	CR 52:2419
15-21	D5S37 D5S644	18	······································	0,22	Testis	GCC 13:249
15-21	D5S644	9 22	3 12	0.33 0.55	Lung	0 12:97 0 12:97
14-21	D5S71	10	1	0.1	Colon	S 241:961
14-21	D5871	ซึ	3	0.1	Colon	CR 50:7166
14-21	D5S71	8	3	0.38	Colon	GCC 3:468
14-21	05971	4	0	0.50	Colon	CCG 48:167
14-21	D5S71	21	1	0.05	Ovarv	IJC 54:546
14-21	D5S71	ĭ	1	ī	Pancreas	GCC 3:466
14-21	D5871	6	0	0	Stomach	GCC 3:468
14-21	D5971	6	2	0.33	Testis	GCC 13:249
14-21	D5S71	***************************************	0	0	Uterus	CR 51:5632
Unknown	D5S409	1 17	1	0.06	Endocrine	CR 56:599
Unknown	D5S409	17	6	0.35	Stomach	CR 56:612
Unknown	D5S409	و ا	6	0.67	Stomach	CR 55:1933
14-21	D5S82	15	4	0.27	Colon	JJCR 82:10
Unknown	D5582	16	1	0.06	Stomach	CR 54:41
21	D5S421	25	5	0.2	Bladder	CR 55:5213
21	_D58421	20	5	0.25	. Read&Neck	CR 54:1152
21	D5S421	5	0	0	Kidney	GCC 12:76
21-22	D5581	13	3	0.23	Cervix	BUC 67:71
Unknown	D5S81	31 5	19	0.61	Colon	CR 50:7166
21-22	D5981		4	0.8	Colon	BJC 67:100
21-22	D5S81	18	4	0.22	Colon	JJCR 82:10
Unknown	D5881	28	5	0.18	Kidney	CR 51:5817
21-22	D5S81	13	3	0.23	Kidney	CR 51:820

Chromosome 5 - q Arm

21-22	D5981	6	•	0.17	Liver	
21-22	D5S81	4	0	0	Liver	
21-22	D5S81	5	1	0.2	Pancreas	BJC 67:100
21-22	D5S81	12	5	0.42	Stomach	HG 92:244
Unknown	D5981	*9	2	0.72	Testis	GCC 13:249
Unknown	L5.71	13	5	0.38	Colon	JJCR 82:10
Unknown	MCC	13	5	9.38	Colon	JJCR 82110
21	MCC	4	1	0.25	Colon	0 9:991
21	MCC	31	. 9	0.29	Colon	CR 52:741
21	MCC	34	12	0.35	Colon	EJC 30A:66
21	MCC	35	22	0.63	Esophageal	Carried to the second
Unknown	L5.71	2	2	1	Lung	CR 52:2478
Unknown	15.71	16	4	0.25	Lung	CR 52:2478
Unknown	L5.71	1	1	1	Lung	CR 52:2478
Unknown	15.71	4	0	- 0	Lung	CR 52:2478
Unknown	MCC	2	2	1	Lung	CR 52:2478
21	MCC	61	9	0.22	Lung	CR. 55:220
Unknown	MCC	1	1	1	Lung	CR 52:2478
Unknown	NCC	. 16	4	0.25	Lung	CR 52:2478
Unknown	MCC	4	0	0	Lung	CR 52:2478
21	MCC	. 7	7	1	Stomach	JJCR 84:10
21	MCC	36	4	0.11	Stomach	CL 96:169
21 21	MCC	. 8	.0	0	Stomach	CR 54:41
1976 100 toxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	MCC-APC	25	7	0.28	Breast	BJC 68:64
21 21	MCC-APC	6	D	0	Cervix	GCC 9:119
21	MCC-APC MCC-APC	45	16	0.36	Colon	GAST 104:1
21	MCC-APC	56	37	0.66	Colon	0 8:1391
Z1 Z1	MCC-APC	26 6	20	0.77	Esophageal	PNAS 89:33
21	MCC-APC	 5	4	0.67	Lung	CR/55:513
21	MCC-APC	7	2	0.4	Lung	CR 52:1996
21	APC	21	7	0.33	Uterus Colon	GCC 9:119 CR 52:741
Unknown	APC	37	3	0.33	Colon	EJC 30A:66
Unknown	APC	33	6	0.18	Colon	EJC 30A:66
21	APC	21	5	0.24	Esophageal	GCC 10:177
21	APC	36	24	0.67	Esophageal	CR 52:6525
21	APC	19	1	0.05	Liver	CR 54:281
21	APC	20	14	0.7	Lung	0 12:97
21	APC	53	17	0.32	Lung	CR 55:220
21	APC	7	5	0.71	Lung	CR 54:1772
21	APC	8	3	0.38	Lung	0.12:97
Unknown	APC	18	9	0.5	Ovarv	GO 55:245
Unknown	APC	15	3	0.2	Prostate	JU 151:107
21	APC	7	3	0.43	Prostate	BJU 73:390
Unknown	APC	13	4	0.31	Stomach	LI 74:835
Unknown	APC	35	3	0.09	Stomach	CL 96:169

Chromosome 5 - q Arm

21	APC	12	Ö	0	Stomach	CR 54:41
21	APC	14	12	0.86	Stomach	JJCR 84:10
21-22	D59346	18	0	0	Endocrine	GCC 13:9
21-22	D55346	46	1	0.02	Kidnev	BJC 69:230
21-22	D5S346	15	6	0.4	Ovary	BJC 69:429
21-22	D5S346	18	2	0.11	Stomach	CR 56:612
21-22	D59346	22	1	0.05	Üterus	CR 54:4294
Unknown	Unknown	19	3	0.16	Colon	JJCR 82:10
Unknown	Unknown	10	2	0.2	Kidney	CR,51:5817
21-22	D5S84	11	2	0.18	Breast	CR 50:7184
21-22	D5884	21	1	0.05	Breast	CR 53:4356
21-22	D5\$84	3	1	0.33	Cervix	GCC 9:119
21-22	D5984	- 8	0	0	Cervix	BJC 67:71
21-22	D5S84	5	2	0.4	Kidney	CR 51:5817
,21-22	D5S84	5	2	0.4	Kidney	CR 51:820
21-22	D5S84	9	4	0.44	Liver	CR 51:89
21- 22	D5984	15	0	0	Ovary	CR:51:5118
21-22	D5S84	13	1	0.08	Uterus	GCC 9:119
21-22	D5586	6.	2	0.33	Colon	GCC 3:468
21-22	D5S86	4	1	0.25	Pancreas	GCC 3:468
21-22	.D5386	8	3	0.38	Stomach	GCC_3:468
31-33	D5S804	19	6	0.32	Ovary	GO 55:245
21-22	FBN2	. 15	6	0.4	Ovary	BJC 69:429
21-22	FBN2	15	4	0.27	Stomach	CR 56:612
33-35	D5970	24	9	0.38	Cervix	CR 54:4481
33-35	D5570	3	0	0	Colon	GCC 3:468
33-35	D5S70	3	. 0	0	Pancreas	GCC.3:468
33-35	D5S70	13	5	0.38	Stomach	GCC 3:468
33-35	05970	13	3	0.23	Testis	0.9:2245
21-22	D5S178	15	6	0.4	Ovary	BJC 69:429
21-22	D55178	19	2	0.11	Stomacb	CR 56:612
31-32	GRL	8	0	0	Ovary	CR 50:2724
21-22	D5S210	15	6	0.4	Ovary	BJC 69:429
21-22	D5S210	19	5	0.26	Stomach	CR 56:612
21-22	D59209	15	6	0,4	Ovary	BJC 69:429
21-22	D5S209	23	2	0.09	Stomacn	CR 56:612
34-qter	D5922	18	0	0	Prostate	G 11:530
34-ater	D5S2	3	1	0.33	Cervix	CR 49:3598
34-gter	D582	2	0	9	Colon	N 331:273
34-qter	D5S2	8	0	0	Liver	JJCR 81:10 PN 84:9252
34-qter	D5S2	. 11	1	0.09	Lung	PN 84:9232
Unknown	D5S2	11	1	0.09	Lung	CR 52:3099
Unknown	D5S2	5	1	0,2	Stomach	CR 48:2988
34-ater	D5S2	2	0	0	Stomach	CR 51:5632
34-qter	D5S2	1	0	0	Uterus	
Unknown	D5S400	32	5	0.16	Cervix	CR 56:197

Chromosome 5 - q Arm

Unknown							
35-qter	Unknown	D5\$429	3	0	- 0	Kidney	PNAS 92:28
35-quer D5843 5 2 0.4 Colon BJC 67:100 BJC 57:100 BJC 57:5755 BJC 59:5755 BJC 59:5755 BJC 59:5755 BJC 59:5755 BJC 59:5755 BJC 59:5755 BJC 59:5755 BJC 59:5755 BJC 59:5755 BJC 59:5755 BJC 59:5755 BJC 59:5755 BJC 67:100 BJ	Unknown	D5S429	19	1	0.05	Kidney	PNAS 92:28
35-qter	35-gter	D5S43	17	1	0.06	Colon	CR 50:7166
35-qter	35-qter	D5\$43	5	2	0.4	Colon	BJC 67:100
DS Section DS Section DS DS DS DS DS DS DS D	35-qter	D5943	31	9	0.29	Colon	BUC: 59:750
35-qter D5543 10 5 0.5 Liver BJC 64:108 35-qter D5943 7 0 0 Pancreas CR 54:2761 35-qter D5943 11 0 0 0 Pancreas DC 63:803 35-qter D5943 10 1 0.1 Stomach BJC 63:803 35-qter D5543 34 8 0.24 Stomach CR 52:2926 35-qter D5943 25 5 0.2 Testis GCC 137:249 35-qter D5943 25 5 0.2 Testis GCC 137:249 Unknown Unknown 17 2 0.11 Brain CR 50:5184 15-21 Unknown 6 0 0 Cervix BJC 67:71 15-21 Unknown 2 1 0.5 Cervix BJC 67:71 15-21 Unknown 11 2 0.18 Cervix BJC 67:71 Unknown Unknown 12 2 0.18 Cervix BJC 67:71 Unknown Unknown 11 2 0.18 Cervix BJC 67:71 Unknown Unknown 13 8 0.35 Colon JUCR 82:10 Unknown Unknown 19 7 0.37 Colon JUCR 82:10 Unknown Unknown 19 7 0.37 Colon JUCR 82:10 Unknown Unknown 1 1 1 Colon JUCR 82:10 Unknown Unknown 10 5 0.13 Colon JUCR 82:10 Unknown Unknown 10 5 0.15 Colon JUCR 82:10 Unknown Unknown 10 5 0.15 Colon JUCR 82:10 Unknown Unknown 10 5 0.15 Colon JUCR 82:10 Unknown Unknown 10 5 0.15 Colon JUCR 82:10 Unknown Unknown 1 1 1 Colon BJC 67:100 Unknown Unknown 1 1 1 Colon BJC 67:100 Unknown Unknown 1 1 1 Colon BJC 67:100 Unknown Unknown 1 1 1 Colon BJC 67:100 21 Unknown 1 1 1 Colon BJC 67:100 21 Unknown 1 1 1 Colon BJC 67:100 21 Unknown 13 1 0.33 Colon S 241:961 21 Unknown 15 4 (0.15 Colon BJC 67:100 21 Unknown D55410 31 1 0.31 Esouhageal GCC 10:177 Unknown D55410 31 1 0.03 HeadSweck CR 54:1756 21 D55140 26 8 0.31 Kidney CR 51:5817 Unknown D1 D1 1 0.1 Urer CR 51:5817 Unknown D1 D1 D1 D1 D1 D1 D1 D	35-qter	D5S43	10	0	0	Endocrine	N 328:524
35 Ger D5943 7	35-gter	D5843	10	3	0.3	Liver	BJC 67:100
35-qter D5S43 11	35-ater	D5S43	10		0.5	Liver	BJC 64:108
35-qter D5543 10 1 0.1 Stomach BUC 59:750	35-gter	D5943	7	0	0	Pancreas	CR 54:2761
35-qter D5543 34 8 0.24 Stomach CR 5\times 2926 35-qter D5543 25 5 0.2 Testis GCC 13;249 Unknown Unknown 12 2 0.17 Brain CR 50;5784 15-21 Unknown 6 0 0 Cervix BJC 67;712 Unknown 2 0 0 Cervix BJC 67;712 Unknown 2 0 0 Cervix BJC 67;712 Unknown Unknown 11 2 0,18 Cervix BJC 67;712 Unknown Unknown 11 2 0,18 Cervix BJC 67;712 Unknown Unknown 11 2 0,18 Cervix BJC 67;712 Unknown Unknown 23 8 0.35 Colon JJCR 82;10 Unknown Unknown 23 8 0.35 Colon JJCR 82;10 Unknown Unknown 29 1 0.5 Colon JJCR 82;10 Unknown Unknown 19 7 0.37 Colon JJCR 82;10 Unknown Unknown 19 7 0.37 Colon JJCR 82;10 Unknown Unknown 17 1 0.06 Colon JJCR 82;10 Unknown Unknown 17 1 0.06 Colon JJCR 82;10 Unknown Unknown 17 1 0.06 Colon JJCR 82;10 Unknown Unknown 17 6 0.35 Colon JJCR 82;10 Unknown Unknown 17 6 0.35 Colon JJCR 82;10 Unknown Unknown 1 1 1 Colon BJC 67;100 JZCR 82;10 Unknown Unknown 1 1 1 Colon BJC 67;100 JZCR 82;10 Unknown Unknown 1 1 1 Colon BJC 67;100 JZCR 82;10 Unknown Unknown 1 1 Colon BJC 67;100 JZCR 82;10 Unknown CRI-145 2 2 0.1 Colon BJC 67;100 JZCR 82;10 Unknown CRI-145 2 2 0.67 Colon BJC 67;100 JZCR 82;10 Unknown CRI-145 2 2 0.67 Colon BJC 67;100 JZCR 82;10 Unknown ERE JZCR J	35-gter	D5S43		0			
35-qter D5943 25 5 0.2 Testis GCC N3;249	35-qter	······································	10	1			
District	35-gter	D5S43					
Unknown	35-gter	D5943	25			***************************************	***************************************
15-21						HORE THE PARTY OF	
21	Compression of the second seco	·····					***************************************
Unknown Unknown 2 1 0.5 Cervix BJC 67:71 Unknown Unknown 11 2 0.18 Cervix BJC 67:71 Unknown Unknown 23 8 0.35 Colon JJCR 82:10 Unknown Unknown 2 1 0.55 Colon JJCR 82:10 Unknown Unknown 19 7 0.37 Colon JJCR 82:10 Unknown Unknown 1 1 1 Colon JJCR 82:10 Unknown Unknown 1 1 1 Colon JJCR 82:10 Unknown Unknown 17 1 0.06 Colon JJCR 82:10 Unknown Unknown 10 5 0.5 Colon JJCR 82:10 Unknown Unknown 17 6 0.35 Colon JJCR 82:10 Unknown Unknown 17 6 0.35 Colon JJCR 82:10 Unknown Unknown 17 6 0.35 Colon JJCR 82:10 Unknown Unknown 1 1 1 1 Colon BJC 67:100 21 Unknown 1 1 1 1 Colon BJC 67:100 21 Unknown 1 1 1 0.33 Colon BJC 67:100 21 Unknown 1 1 1 0.33 Colon RJCR 1:00 21 Unknown CRT-11265 16 1 0.35 Colon S 241:951 Unknown CRT-145 21 2 0.1 Colon S 241:961 33 CGFIR 11 4 0.36 Colon S 241:961 21 D5S141 3 2 0.67 Colon S 241:961 21 D5S141 3 2 0.67 Colon BJC 67:100 Unknown EMS 9 2 0.22 Colon N 3JRC 7:100 Unknown EMS 9 2 0.22 Colon N 3JRC 7:100 Unknown D5S410 31 1 0.03 HeadéNeck CR 54:4756 Unknown D5S410 35 4 0.11 HeadéNeck CR 54:4756 Unknown D5S410 35 4 0.11 HeadéNeck CR 54:4756 Unknown D5S410 35 4 0.11 HeadéNeck CR 54:4756 Unknown D5S410 35 4 0.11 HeadéNeck CR 54:4756 Unknown D5S410 35 4 0.11 HeadéNeck CR 54:4756 Unknown D5S410 35 4 0.11 HeadéNeck CR 54:4756 Unknown D5S410 35 5 0.13 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 21 D5S140 16 3 0.19 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817							***********
Unknown Unknown 11	***************************************		***************************************	***********			*******************
Unknown					COMMAND AND DESCRIPTION OF THE PROPERTY AND THE PROPERTY OF TH	*******************	THE RESERVE OF THE PARTY OF THE
Onknown Unknown 2 1 0.5 Cglon JUCR 82:10 Unknown Unknown 19 7 0.37 Colon JJCR 82:10 Unknown Unknown 1 1 1 Colon JJCR 82:10 Unknown Unknown 17 1 0.06 Colon JJCR 82:10 Unknown Unknown 17 6 0.35 Colon JJCR 82:10 Unknown Unknown 1 1 1 Colon JJCR 82:10 Unknown Unknown 1 1 1 Colon JJCR 82:10 21 Unknown 1 1 1 Colon JJCR 82:10 21 Unknown 1 1 1 Colon JJCR 82:10 21 Unknown 1 1 1 Colon JJCR 82:10 Unknown CRI-12 3 0 0.75 Colon BJC 67:100 21 Unknown CRI-1265 16 </td <td>The state of the s</td> <td></td> <td>····</td> <td></td> <td></td> <td>************</td> <td>***************************************</td>	The state of the s		····			************	***************************************
Unknown Unknown 19 7 0.37 Colon JJCR 82:10 Unknown Unknown 1 1 1 Colon JJCR 82:10 Unknown Unknown 17 1 0.06 Colon JJCR 82:10 Unknown Unknown 10 5 0.35 Colon JJCR 82:10 Unknown Unknown 17 6 0.35 Colon JJCR 82:10 Unknown Unknown 3 0 0 Colon JJCR 82:10 Unknown Unknown 1 1 1 Colon JJCR 82:10 Z1 Unknown 4 3 0.75 Eolon BJC 67:100 Z1 Unknown CRI-11265 16 1 0.06 Colon S 241:961 Unknown CRI-145 21 2 0.1 Colon S 241:961 33 C9FIR 11 4 0.35 Colon CR 50:7166 21 D5S141	Commence of the property of the commence of th	******					and the second and second and the second second second
Unknown Unknown 1 1 1 1 Colon JJCR 82:10 Unknown Unknown 17 1 0.06 Colon JJCR 82:10 Unknown Unknown 10 5 0.5 Colon JJCR 82:10 Unknown Unknown 17 6 0.35 Colon JJCR 82:10 Unknown Unknown 3 0 Colon JJCR 82:10 15-21 Unknown 1 1 1 Colon JJCR 82:10 21 Unknown 1 1 1 Colon JJCR 82:10 21 Unknown 4 3 0.75 Colon BJC 67:100 21 Clipi 3 1 0.33 Colon N 331:273 Unknown CRI-145 1 2 0.1 Colon S 241:961 33 CSFIR 11 4 0.95 Colon S 241:961 33 CSFIR 1 4 0	**************************************		~~~~~	***************************************	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	**********	***************************************
Unknown Unknown 17 1 0.06 Colon JJCR 82:10 Unknown Unknown 10 5 0.5 Colon JJCR 82:10 Unknown Unknown 17 6 0.35 Colon JJCR 82:10 Unknown 3 0 0 Colon JJCR 82:10 21 Unknown 1 1 1 Colon JJCR 82:10 21 Unknown 4 3 0.75 Colon BJC 67:100 21 Unknown 4 3 0.75 Colon BJC 67:100 21 Clipil 3 1 0.33 Colon S 241:961 Unknown CRI-L45 21 2 0.1 Colon S 241:961 33 CSF1R 11 4 0.36 Colon S 241:961 33 CSF1R 13 4 0.36 Colon BJC 67:100 21 D5S141 3 2 0.67 Colo	· · · · · · · · · · · · · · · · · · ·	THE STREET STREET	····	THE RESIDENCE OF THE PARTY OF T			
Unknown Unknown 10 5 0.5 Colon JJCR 82:10 Unknown Unknown 17 6 0.35 Colon JJCR 82:10 Unknown Unknown 3 0 .0 Colon JJCR 82:10 15-21 Unknown 1 1 1 Colon BJC 67:100 21 Unknown 4 3 0.75 Colon BJC 67:100 21 Clipil 3 1 0.33 Colon BJC 67:100 21 Clipil 3 1 0.06 Colon S:241:961 Unknown CRI-1265 16 1 0.06 Colon S:241:961 Unknown CRI-145 21 2 0.1 Colon S:241:961 33 CSFIR 11 4 0.35 Colon S:241:961 21 D5S141 3 2 0.67 Colon R:50:7166 21 D5S141 35 3 <t< td=""><td>Commission of the control of the con</td><td>****************</td><td>~~.~</td><td></td><td></td><td>Company of the Control of the Contro</td><td></td></t<>	Commission of the control of the con	****************	~~.~			Company of the Control of the Contro	
Unknown Unknown 17 6 0.35 Colon JJCR 82:10 Unknown Unknown 1 1 1 1 Colon BJC 67:100 21 Unknown 4 3 0.75 Colon BJC 67:100 21 Clipil 3 1 0.33 Colon N 331:273 Unknown CRI-11265 16 1 0.06 Colon S:241:961 Unknown CRI-145 21 2 0.1 Colon S:241:961 Unknown CRI-145 21 2 0.1 Colon S:241:961 33 CSFIR 11 4 0.36 Colon S:241:961 21 D5S141 3 2 0.67 Colon BJC 67:100 Unknown FMS 9 2 0.22 Colon N:331:273 21-22 LS5.34 5 3 0.6 Colon CR 50:7166 21 D5S141 35	CONTRACTOR OF CO	CONTRACTOR OF THE PROPERTY OF			CONTRACTOR OF THE PROPERTY OF		Martin Cartering and American Services A.
Unknown Unknown 1	Contraction of the Contraction o					AND DESCRIPTION OF THE PARTY OF	
15-21	Company of the Compan						· The contract of the contract of the course.
21 Unknown 4 3 0.75 Colon BJC 67:100 21 C11p11 3 1 0.33 Colon N 331:273 Unknown CRI-L1265 16 1 0.06 Colon S 241:961 Unknown CRI-L45 21 2 0.1 Colon S 241:961 33 CSFIR 11 4 0.36 Colon CR 50:7166 21 D5S141 3 2 0.67 Colon BJC 67:100 Unknown FMS 9 2 0.22 Colon N 331:273 21-22 L55.34 5 3 0.6 Colon D 33:273 21-22 L55.34 5 3 0.6 Colon CR 50:7166 21 D5S141 35 13 D.37 Esophageal GCC 10:177 Unknown D5S410 31 1 0.03 Head&Neck CR 54:4756 21 D5S133 6 1	TO A STATE OF THE PARTY OF THE	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	···			*************	····
C1	The second section of the second seco	Control of the Contro	***********************************				
Unknown CRI-11265 16 1 0.06 Colon S.241:961 Unknown CRI-145 21 2 0.1 Colon S.241:961 33 CSFIR 11 4 0.36 Colon CR 50:7166 21 D5S141 3 2 0.67 Colon BJC 67:100 Unknown FMS 9 2 0.22 Colon N 331:273 21-22 LS5.34 5 3 0.6 Colon CR 50:7166 21 D5S141 35 13 0.37 Escphageal GCC 10:177 Unknown D5S410 31 1 0.03 Head&Neck CR 54:4756 21 D5S133 6 1 0.11 Read&Neck CR 54:4756 21 D5S140 16 3 0.19 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 Unknown D5S89 15).03.000.000.000.000.000.000.000.000.000	******************************	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	***************************************	(% 04mm) 2000 page 400 page ; 3.000 page 3.0	***************************************	Separation of the second of th
Unknown CRI-L45 21 2 0.1 Colon S 241:961 33 CSFIR 11 4 0.36 Colon CR 50:7166 21 D5S141 3 2 0.67 Colon BJC 67:100 Unknown FMS 9 2 0.22 Colon N 331:273 21-22 LS5.34 5 3 0.6 Colon CR 50:7166 21 D5S141 35 13 0.37 Escphageal GCC 10:177 Unknown D5S410 31 1 0.03 Head&Neck CR 54:4756 21 D5S133 6 1 0.17 Kidney CR 51:5817 21 D5S140 16 3 0.19 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 Unknown D5S89 15 5 0.33 Leukemia B B3:199 Unknown Unknown 6 0 <td>- consequence representation of the consequence of</td> <td>KONSTITUTORES CONTRACTOR CONTRACT</td> <td></td> <td></td> <td></td> <td>**************************************</td> <td>CONTRACTOR OF THE PROPERTY OF</td>	- consequence representation of the consequence of	KONSTITUTORES CONTRACTOR CONTRACT				**************************************	CONTRACTOR OF THE PROPERTY OF
33 CSFIR 11 4 0.36 Colon CR 50:7166	\$1000 de la company de la comp	A MANAGEMENT AND A CONTRACT OF THE PARTY OF	***		***************************************	***************************************	**************************************
21 D5S141 3 2 0.67 Colon BJC 67:100		*****	(0.00) / 0.000000000000000000000000000000	*********		***************************************	CR 50:7166
Unknown FMS 9 2 Q.22 Colon N.331:273 21-22 LS5.34 5 3 0.6 Colon CR 50:7166 21 D5S141 35 13 0:37 Esophageal GCC:10:177 Unknown D5S410 31 1 0.03 Head&Neck CR 54:4756 Unknown D5S410 35 4 0:11 Head&Neck CR 54:4756 21 D5S133 6 1 0.17 Kidney CR 51:5817 21 D5S140 16 3 0.19 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 Unknown D5S89 15 5 0:33 Leukemia B B3:199 Unknown Unknown 10 1 0.1 Liver CR 51:89 21 Unknown 6 0 0 Liver BJC:67:100	***************************************		***************************************			******************	BJC 67:100
21-22 L55.34 5 3 0.6 Colon CR 50:7166 21 D5S141 35 13 0.37 Esophageal GCC:10:177 Unknown D5S410 31 1 0.03 Head&Neck CR 54:4756 Unknown D5S410 35 4 0.11 Head&Neck CR:54:4756 21 D5S133 6 1 0.17 Kidney CR 51:5817 21 D5S140 16 3 0.19 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 Unknown D5S89 15 5 0.33 Leukemia B 83:199 Unknown Unknown 10 1 0.1 Liver CR 51:89 21 Unknown 6 0 0 Liver BJC:67:100	and the second s	**************************************	9		0.22	Colon	N 331:273
21 D5S141 35 13 D.37 Esophageal GCC 10:177	(300MV800Acres advantages acres version Acres seguences					Colon	CR 50:7166
Unknown D5S410 31 1 0.03 Head&Neck CR 54:4756 Unknown D5S410 35 4 0.11 Head&Neck CR 54:4756 21 D5S133 6 1 0.17 Kidney CR 51:5817 21 D5S140 16 3 0.19 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 Unknown: D5S89 15 5 0.33 Leukemia B 83:199 Unknown Unknown 10 1 0.1 Liver CR 51:89 21 Unknown 6 0 0 Liver BJC 67:100	71	D5S141			0.37	Esophageal	GCC 10:177
21 D5S133 6 1 0.17 Kidney CR 51:5817 21 D5S140 16 3 0.19 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 Unknown: D5S89 15 5 0:33 Leukemia B 83:199 Unknown Unknown 10 1 0.1 Liver CR 51:89 21 Unknown 6 0 0 Liver BJC 67:100		the water water and the second water the second sec			0.03		CR 54:4756
21 D5S133 6 1 0.17 Kidney CR 51:5817 21 D5S140 16 3 0.19 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 Unknown: D5S89 15 5 0:33 Leukemia B 83:199 Unknown Unknown 10 1 0.1 Liver CR 51:89 21 Unknown 6 0 0 Liver BJC 67:100	Unknown	D59410		4	0.11	Head&Neck	CR 54:4756
21 D5S140 16 3 0.19 Kidney CR 51:5817 21 D5S141 26 8 0.31 Kidney CR 51:5817 Unknown; D5S89 15 5 0.33 Leukemia B B3:199 Unknown Unknown 10 1 0.1 Liver CR 51:89 21 Unknown 6 0 0 Liver BJC:67:100	21	D5S133		1	0.17	Kidney	CR 51:5817
21 D5S141 26 8 0.31 Kidney CR 51:5817 Unknown D5S89 35 5 0:33 Leukemia B B3:199 Unknown Unknown 10 1 0.1 Liver CR 51:89 21 Unknown 6 0 0 Uiver BJC 67:100	21	D5S140		3	0.19	Kidney	
Unknown D5S89 15 5 0:33 Leukemia B 83:199 Unknown Unknown 10 1 0.1 Liver CR 51:89 21 Unknown 6 0 0 Liver BJC 67:100				8	***************************************	Kidney	CR 51:5817
Unknown Unknown 10 1 0.1 Liver CR 51:89 21 Unknown 6 0 0 Liver BJC 67:100	Unknown	CONTRACTOR OF THE PROPERTY OF	15	5	0.33	Leukemia	B 83:199
		Unknown	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	***************************************	0.1	Liver	CR 51:89
45 100	21	Unknown	6	0	0	Liver	***************************************
		Unknown	5	С	0	Liver	BJC 67:100

Chromosome 5 - q Arm

21	D5S141	7	0	0	Liver	BJC 67:100
21-21-34-gter	D5S43-D5S81	45	14	0.31	Liver	JJCR 84:89
21	ECB27	- 8	1	0.12	Liver	BJC 64:108
Unknown	FMS	2	0	. 0	Lung	PN 84:9252
13-12	de1-27	15	11,	0.73	Lung	0 12:97
13-12	de1-27	8	3	0.38	Lung	0 12:97
13-12	de1-27	7.	4	0.57	Lung	CR 54:1772
21	D5S122	11	5	0.45	Ovary	GO 55:245
Unknown	D5S6-D59107-APC	37	16	0,43	Ovary	CR 53:2393
21-22	IRF-1	15	66	0.4	Ovary	BJC 69:429
15-21	Unknown	5	0	0	Pancreas	BJC 65:809
15-21	D5S98	13	3	0.23	Stomach	HG 92:244
21-22	IRF-1	22	6	0.27	Stomach	CR 56:612
15-21	D5S98	7	1	0.14	Testis	GCC 13:249
Unknown	FMS	21-	1	0.05	Uterus	CR 54:4794
SUM		2866	763	0.27		

Chromosome 6 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
Unknown	D6S477	33	15	0.45	Colon	CR 56:145
24-25	F13A1	18	5	0.28	Ovary	GO 55:245
24-25	F13A1	18	4	0.22	Ovary	BJC 69:429
Unknown	D6S309	18	1	0.06	Kidney	PNAS 92:2854
Unknown	D6S309	4	1	0.25	Kidney	PNAS 92 2854
pter-p25	D6F21S1	12	4	0.33	Ovary	BJC 67:551
Unknown	D6S89	14	1	0.07	Ovary	BJC 67:551
Unknown	D6S289	36	13	0.36	Colon	CR 56:145
Unknown	D6S260	32	14	0.44	Cervix	CR 56:197
21.3-24	D65109	17	3	0.18	Ovary	BJC 69:429
21.3-24	D65109	1.6	.2	0.12	Oterus	CR 54:4294
Unknown	D6S276	20	10	0.5	Cervix	CR 56:197
Unknown	D6S299	21	1	0.05	Head&Neck	CR.56:47567
Unknown	D6S299	20	0	0	Head&Neck	CR 54:4756
Unknown	D68288	26	2	0.08	Melanoma:	CR 56:589
Unknown	D6S105	27	2	0.07	Esophageal	IJC 69:1
Unknown	D6S105	19	4	0.21	Head&Neck	CR 54:1152
Unknown	D6S105	26	2	0.08	Uterus	CR 54:4294
Unknown	D63258	33	15	0.45	Colon:	CR 56:145
Unknown	D6S10	35	4	0.11	Breast	GCC 2:191
Unknown	D6810	32	9	0.28	Cervix	CR 54:4481
Unknown	D6S10	2	0	0	Pancreas	CR 54:2761
Unknown	D6S10	13	0	0	Prostate	G 11:530
Unknown	D6S10	32	4	0.12	Testis	0 9:2245
21.3	HLA-DRB	21	3	0.14	Ovary	BJC 67:551
21.3	HLA-DQA	18	4	0.22	Ovary	BJC 67:551
21.3	HLA-DQA	3 .	<u>.</u> 0	0	Testis	CCG 52:72
21.3	HLA-DQA	1	0	0	Testis	CCG 52:72
21.3	BLA-DQA	****	0	<u>0</u>	<u>Testis</u>	CCG 52:72
Unknown	TNFa	33	14	0.42	Colon	CR 56:145
Unknown Unknown	D65291	12	1	0.08	Brain	CR 55:4696
CONTRACTOR CONTRACTOR CONTRACTOR	D6S291 D6S29	12 17	1 0	0.08 0	Brain	CR 55:4696 CCG:48:167
Unknown Unknown	D6529	22		************************	Colon Kidney	CR 51:5817
Unknown	D6S29	13	3 1	0.14	Liver	CR 51:89
Unknown	D6529	12		0.5	Ovary	CR 51:5118
Unknown	D6529	19	6 4	0.3	CONTRACTOR OF THE PARTY OF THE	TJC 54:546
Unknown	D6S29	9	0	0	Ovary Ovary	CR 50:2724
Unknown	D6S29	16	3	0.19	Stomach	GCC 14:28
Unknown	D6S271	44	17	0.39	Colon	CR 56:145
Unknown	D6S282	32	6	0.39	Cervix	CR 56:197
Unknown	D65282	22	0	0.13	Endocrine	CR 56:599
12.0-11	KRAS P1	. 8	1	0.12	Ovary	BJC 67:551
12.0-11	KRAS Pl	2	0	0.12	Uterus	CR 51:5632
11.2	D6S294	37	11	0,3	Ovary	GCC 15:273
Unknown	D6S257	42	13	0.31	Colon	CR 56:145
CITATIONII	503251	4 4	T-3	0.51	C010!!	J., J., 1.

Chromosome 6 - p Arm

Unknown D6S257 42 13 0.31 Unknown Unknown 14 1 0.07 Unknown D6S40 24 2 0.08 Unknown D6S40 28 5 0.18 Unknown D6S40 3 1 0.33 Unknown D6S344 22 0 0 Unknown D6S139 49 12 0:24 Unknown D6S40 23 7 0.3 Unknown D6S40 14 1 0:07 Unknown D6S265 19 8 0.42 Unknown TCTE 14 2 0:14	Brain Brain Breast Cervix Endocrine Esophageal Esophageal Head&Neck Head&Neck Kidney	CR 56:599 GCC 10:177 CR 54:2996
Unknown D6840 24 2 0:08 Unknown D6840 28 5 0.18 Unknown D6840 3 1 0:33 Unknown D68344 22 0 0 Unknown D68349 49 12 0:24 Unknown D6840 23 7 0.3 Unknown D6840 14 1 0:07 Unknown D68265 19 8 0.42 Unknown TCTE 14 2 0:14	Brain Breast Cervix Endocrine Esophageal Esophageal Head&Neck Head&Neck Kidney	CR 49:6577 CR 50:7184 GCC 9:189 CR 56:599 GCC 10:177 CR 54:2996 CR 51:2113 CR 54:1152
Unknown D6S40 28 5 0.18 Unknown D6S40 3 1 0.33 Unknown D6S344 22 0 0 Unknown D6S139 49 12 0.24 Unknown D6S40 23 7 0.3 Unknown D6S40 14 1 0.07 Unknown D6S265 19 8 0.42 Unknown TCTE 14 2 0:14	Breast Cervix Endocrine Esophageal Esophageal Head&Neck Head&Neck Kidney	CR 50:7184 GCC 9:189 CR 56:599 GCC 10:177 CR 54:2996 CR 51:2173 CR 54:1152
Unknown D6S40 3 1 0.33 Unknown D6S344 22 0 0 Unknown D6S39 49 12 0.24 Unknown D6S40 23 7 0.3 Unknown D6S40 14 1 0.07 Unknown D6S265 19 8 0.42 Unknown TCTE 14 2 0.14	Cervix Endocrine Esophageal Esophageal Esophageal Head&Neck Head&Neck Kidney	GCC 9:119 CR 56:599 GCC 10:177 CR 54:2996 CR 51:2113 CR 54:1152
Unknown D6S344 22 0 0 Unknown D6S139 49 12 0.24 Unknown D6S40 23 7 0.3 Unknown D6S40 14 1 0.07 Unknown D6S265 19 8 0.42 Unknown TCTE 14 2 0:14	Endocrine Esophageal Esophageal Esophageal Head&Neck Head&Neck Kidney	CR 56:599 GCC 10:1/17 CR 54:2996 CR 51:21/3 CR 54:1152
Unknown D6S139 49 12 0.24 Unknown D6S40 23 7 0.3 Unknown D6S40 14 1 0.07 Unknown D6S265 19 8 0.42 Unknown TCTE 14 2 0.14	Esophageal Esophageal Head&Neck Head&Neck Kidney	GCC 10:177 CR 54:2996 CR 51:2113 CR 54:1152
Unknown D6540 23 7 0.3 Unknown D6540 14 1 0.07% Unknown D65265 19 8 0.42 Unknown TCTE 14 2 0:14	Esophageal Esophageal Head&Neck Nead&Neck Kidney	CR 54:2996 CR 51:2113 CR 54:1152
Unknown D6S40 14 1 0:07 Unknown D6S265 19 8 0.42 Unknown TCTE 14 2 0:14	Fsophageal- Head&Neck Head&Neck Kidney	CR 51:2113 CR 54:1152
Unknown D6S265 19 8 0.42 Unknown TCTE 14 2 0.14	Head&Neck Head&Neck Kidney	CR 54:1152
Unknown TCTE 14 2 0:14	Head&Neck Kidney	***************************************
	Kidney	CR 54:1152 2 1
21.3 D65138 34 6 0.18		
3, 0 0.16		CR 51:5817
	Kidney	CR 51:5817
Unknown D6S4-C2-D6S1 19 5 0.26	Kidney	CR 49:5087
Upknown D6540 I4 3 0.21	Kidney	CR 51:820-0
<u>Unknown</u>	Lung	CR 54:2322
Unicrown: D694-C72-D691 1 1 1	Lung	CR 49:5087
Unknown D6S40 22 4 0.18	Lung	CR 52:2478
<u>24-27 Onknown 7 2 0.29</u>	Ovary	0 5:219
Unknown	Ovary	BJC 67:551
Unknown D6S40 7 4 0.57	Ovary	0 5:219
Unknown F13A1- D6S249 17 4 0.24	Ovary	BJC 72:1330
12-21.3 FTHP1 14 5 0.36	Ovary	BJC 69:429
12-21.2 FTHP1 10 2 0.2	Ovary	BJC 67:551
Unknown PIM-HLA-D6S91- 34 21 0.62	Ovary	CR 53:2393
D6541		
Unknown D6S4-C2-D6S1 2 1 0.5	Sarcoma	CR 49:5087
Unknown D6S40 L3 7 0.54	Sarcoma	CR 52:2419
21.3 HLA-DXA 2 0 0	Testis	CCG 52:72
21.3 ALA-DXA 2 0 0	Testis	CCG 52:72
21.3 HLA-DXA 1 0 0	Testis	CCG 52:72
Uaknown D6S40 5 0 0	Uterus	GCC 9:119
SUM 1383 328 0.24		DANGE CONTRACTOR OF THE PROPERTY OF THE PROPER

Chromosome 6 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
Onknown	D621	8	2 .	0.25	Ovary.	BJC 67:551
Unknown	D6Z1	22	0	0	Stomach	GCC 14:28
13	D69313	30	3	0.1	Breast	BJC"71:290
13	D6S254	5	0	0	Breast	BJC 73:144
13	D65280	20	8	0.4	Breast	BJC:71:290
14-15	D6S284	26	5	0.19	Breast	BJC 71:290
14-15	D9S284	5	1	0.2	Breast	BJC-73:144
16.3-21	D65286	27	8	0.3	Breast	BJC 71:290
14-15	D65286	11	4	0:36	Breast	BJC 73:144
16.3-21	D6S286	17	1	0.06	Endocrine	CR 56:599
14-15	D69286	17	6 .	0.47	Ovary	GCC:15:223
Unknown	EDDR1	14	4	0.29	Ovary	GCC 15:223
22.3-23.1	D65270	5	1	0.2	Breast	
22.3-23.1	D6S270	22	7	0.32	Ovary	GCC 15:223
Unknown	D68310	23	7.	0.:3	Endocrine	
Unknown	D65310	33	10	0.3	Ovary	GCC 15:223
Onknown	D65311	27	- 5	0.19		CR 56:197
Unknown	D65311	6	4	0.67	Endocrine	
Unknown	D69311	32	10	0.31	ACTION AND ADDRESS	CR 56:599
Unknown	D6S194	4	0		Ovary	GCC 15;223
Onknown	D65194	16	5	0	Ovary	CR 52:5815
Unknown	D6S194	16		0.31	Ovary	GCC_15:223
Unknown	D69142	30	4 8	0.25	Ovary	CR 52:5815
Unknown	D65142	6		0.27	Kidney	CR 51:5817
Caknown	D6S142	12	<u> </u>	0	Ovary	CR 52:5815
Unknown	D6S142	6	***************************************	0.58	Ovary	CR 52:5815
Unknown	D6S161	27	0	0	Ovary	CR 52:5815
Unknown	D6S161		6	0.22	Kidney	CR 51:5817
Onknown	TO STATE OF THE PARTY OF THE PA	11	0 7	0	Ovary	CR 52:5815
Unknown	D65161	17	·····	0.41	Ovary	CR 52:5815_
CONTROL OF CONTROL OF	D6S161	5	1	0.2	Ovary	CR 52:5815
Unknown	D69251	67	16	0.24	Breast	BJC [73:144]
Unknown	D6S251	36	13	0.36	Colon	CR 56:145
Onknown	D65251	5	0	<u>, , , , , , , , , , , , , , , , , , , </u>	Overy	CR:55:2169
Unknown	D6S251	28	0	0	Ovary	CR 55:2169
13	D6S239	27	9	0.33	Breast	BJC 71:290
13	D6S239	10	33	0.3	Ovary	CR 55:2169
13	D65239	27	1	0.04	Overy	CR 55:2169
14-16.2	D6S252	48	11	0.23	Breast	BJC 73:144
14-16.2	D69252	27	2	0.07	Stomach	GCC 14:28
14	D6S300	32	11	0.34	Breast	BJC 71:290
14	D6\$300	17	3	0.18	Endocrine	CR 56:599
16.3	D6S246	27	9	0.33	Breast	BJC 71:290
Unknown	D6S246	16	1	0:06	Ovary	CR 55:2169
Unknown	D6S246	9	2	0.22	Ovarv	CR 55:2169
16.3-21	.D6\$249	.28	9	0.32	Breast	BJC:73:144
16.3-21	D6 S2 83	30	5	0.17	Breast	BJC 71:290
			=		21000	230 .1.230

Chromosome 6 - q Arm

16.3-21	D69283	10	2	0.2	Stomach	GCC 14:28
Unknown	D6S268	4	1	0.25	Kidney	GCC 12:76
Unknown	D6S268 - **	9	7	0.71	Stomach	GCC 14:28
16.3-21	D6S302	30	13	0.43	Breast	BJC 73:144
71-23.3	D69261	34	7	0.21	Breast*	BJC 71:290
21-23	D6S261	25	5	0.2	Breast	BJC 73:144
21-23	D6S287	33	4	.0.12	Breast	BJC 73:144
21-23	D6S287	22	4	0.18	Endocrine	CR 56:599
Unknown	D69267	18	5	0.28	Ovary	GCC 15: 723 %
22.3-23.1	ARG	12	2	0.17	Breast	BJC 73:144
22.3-23.1	ARG	15	0	0	Stomach	GCC 14:28
22.3-23.1	D6S262	28	10	0.36	Breast	BJC 73:144
Unknown	D69262	35	12	0.34	Colon	CR 56:145
Unknown	D6S262	17	1	0.06	Head&Neck	CR 54:4756
Unknown	D6S252	21	3	0.14	ReadsNeck	CR 5414756
Unknown	D6S32	18	9	0.5	Stomach	GCC 14:28
23.1	D6S87	17	. 6	0.35	Ovary	BJC 69:429
23.1	D6S87	18	3	0.17	Ovary	CR 55:2169
23.1	D6587	7	2	0.29	Ovary	CR 55:2169
23.1	D6S87	20	1	0.05	Uterus	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
22-23	MYB	10	0	0.03	CONTRACTOR AND ADDRESS OF THE PROPERTY OF THE	CR 54:4294
22-23	MYB	11	2		<u>Cervix</u>	CR 49:3598
22-23	MYB	20	2	0.18	Colon	N 331:273
22-23	MYB	13	<u>4</u> 23	0.1	Colon	IJC 53:382
22-23	MYB	18	3	0.17	Liver	JJCR 81:108
22-23	MYB	7		~~~ ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Lung	PN 84:9252
22-23	MAB	5	3	0.43	Melanoma	CR 51:5449
	rilo.		0	U	Neuroblasto a	m CR 49:1095
22-23	MYB	9	6	0.67	Ovary	BJC 67:551
22-23	MYB	4	i	0.25	Qvary	GO 55:245
22-23	MYB	8	1	0.12	Ovary	CR 50:2724
22-23	MYB	7	ò	0.12	Prostate	G 11:530
22-23	MYB	20	6	0.3	Sarcoma	CR 52:2419
22-23	MYB	12	1	0.08	CONTRACTOR OF COLUMN PARKET CONTRACTOR CONTR	GCC 14:28
22-23	MYB	13	~~~~	0	Stomach	
22-23	MXB	12	0 2	TORRESON OF THE PROPERTY OF TH	Stomach	CR 48:2988
22-23	MYB		***************************************	0.17	Stomach	CR 52:3099
Unknown	processing processing of the contraction of the con	7	1	0.14	Uterus	CR 51:5632
Unknown	D6\$250	24	1	0.04	Ovary	CR 55:2169
	D6S250	10	3	0.3	Ovary	CR 55:2169
Unknown	D69136	16	2	0.12	Kidney	CR 51:5817
Unknown	D6S136	3	0	0	Ovary	CR 52:5815
Unknown	D6\$136	9	0	- 0	Ovary	CR 52:5815
Unknown	D6S441	11	1	0.09	Endocrine	CR 56:599
Unknown	D69441	. 30	13	0,43	Ovary	GCC 15:223
24-27	ESR	16	0	0	Cervix	CGC 79:74
24-27	ESR	8	3	0.38	Colon	GCC 3:468
24-27	ESR	8	4	0.5	Melanoma	CR 51:5449

Chromosome 6 - q Arm

24-27	ESR	23	6	0.26	Ovary	CR 55:2169
24-27	ESR	6	1	0.17	Ovary	CR 55:2169
24-27	<u> F9R</u>	13		0.15	Ovary	GO 47:137
24-27	ESR	14	9	0.64	Ovary	CR 50:2724
24-27	ESR	22	12	0,05	Ovary	IJC 54:546**
24-27	ESR	15	10	0.67	Ovary	BJC 67:551
24-27	ESR	18	10	0.56	Cvary	GCC 15:223
24-27	ESR	1	1	1	Pancreas	GCC 3:468
24-27	ESR	- 6	0	0	Stomach	GCC 3:468
24-27	ESR	16	0	0	Stomach	CR 51:2926
24-27	ESR	6	1	0.17	Oterus	CR 51:5632
Unknown	D6S415	22	9	0.41	Ovary	GCC 15:223
25.2	D69255	9		0.33	Breast	BJC 73:144
25.2	D6S255	23	2	0.09	Head&Neck	CR 54:1152
25.2 25.2	D65255		3	0.43	Ovary	CR 55:2169
Unknown	D6S255 D69305	11 29	2	0.18	Ovary	CR 55:2169
Unknown	D6S305	*************************	.4:	0.14	Cervix;	CR 56:197
Unknown	D6S305	40 15	16	0.4	Colon	CR 56:145
Unknown	D6S305	29	<u>. 2</u> 9	0.13	Endocrine	CR 56:599
Unknown	D6S305	35	13	0.31	Melanoma	CR 56:589
Unknown	IGF2R	16	13 11	0.37	Ovary	GCC 15:223
Unknown	IGF2R	7	0	0.69 0	Liver	0 10:1725
Unknown	IGF2R	4	1	0.25	Overy	CR 55:2169
Unknown	IGF2R	18	5	0.23	Ovary Ovary	CR 55:2169
Unknown	IGF2R	11	3	0.27	Ovary	CR 55:2169
Unknown	IGF2R	7	Ō	0.27	Ovary	CR 55:2169
Unknown	IGF2R	18	2	0.11	Stomach	GCC 14:28
Unknown	IGF2R	10.	2	0.2	Uterus	CR 54:4294
26-27	PLG	2	0	0	Liver	PNAS 86:8852
Unknown	D6S195	14	5	0.36	Ovary	CR 52:5815
Unknown	D6S195	2	0	0	Ovarv	CR 52:5815
Unknown	D69195	5	0	0	Ovary	CR 52:5815
Unknown	D65191	16	3	0.19	Ovarv	CR 52:5815
Unknown	D6S191	5	0	0	Overy	CR 52:5815
Unknown	D6S191	8	0	0	Ovary	CR 52:5815
26	D69186	25	5	0.2	Breast	BJC 71:290
26	D65186	34	7	0.21	Kidnev	CR 51:5817
26	D6S186	19	8	0.42	Ovary	CR 52:5815
26	D6S186	19	8	0.42	Ovary	GCC 15:223
26	D69186	6	1	0.17	Ovary	CR 52:5815
26	D6S186	5	0	0	Ovary	CR 52:5815
Unknown	SOD2	11	3	0.27	Melanoma	CR'51:5449
Unknown	SOD2	9	4	0.5	Ovary	BJC 67:551
Unknown	SOD2	23	. 5	0.22	Stomach	GCC 14:28
Unknown	D6S264	32	13	0.41	Colon	CR 56:145

Chromosome 6 - q Arm

Unknown	D69264	12	. 5	0.42	Endocrine	CR 56-599
Unknown	D6S264	15	5	0.33	Head&Neck	CR 54:1152
Onknown	D68264	3	1	0.33	Kidney	GCC 12:76
Unknown	D6S264	34	12	0.35	Ovary	GCC 15:223
Unknown	D69503 -	34	14.	0.41	"Colon"	CR 567145
21-gter	D6S2	8	3	0.38	Colon	GCC 3:468
21-qter	D&S2	19	4	0.21	Ovary	IJC 52:575
21-gter	D6S2	5	3	0.6	Ovary	0 5:219
21-qter	D692	- 21	1.	0.05	Ovary	IJC 54:546 WE
21-gter	D6S2	1	1	1	Pancreas	GCC 3:468
21-gter	D6S2	6	0	0	Stomach	GCC 3:468
Unknown	D6S133	22	14	0.64	Ovary	BJC 67:551
Unknown	D69193	56	9	.01.16	Esophageal	GCC*10:177
Unknown	D6S193	38	23	0.61	Ovary	GCC 15:223
27	D6S297	19	4	0.21	Breast	BJC 71-290
Unknown	D6S297	27	14	0.52	Ovary	GCC 15:223
<u>Unknown</u>	TCP10	17	12	0.71	Ovary	BUC 67/1551
27	D6S44	56	4	0.07	Breast	CR 53:4356
27	D6944	12	. 4	0.33	Breast	GCC 2-191
27	D6S44	29	4	0.14	Ovary	IJC 54:546
27	D6S44	18	. 0	0	Testis	LI 73:606
Unknown	D6S149	19	6	0.32	Ovary	GCC 15:223
Onknown	D6S149	8	2	0.25	Ovary	CR 52:5815
Unknown	D6S149	9	1	0.11	Ovary	CR 52:5815
Unknown	D69149	22	10	0.45	Ovary	CR 52:5815
Unknown	D6S37	4	1	0.25	Breast	CR :53:3804
Onknown	D6937	23	2	0.09	Breast	CR 50:7184
Unknown	D6S37	20	4	0.2	Cervix	CR 54:4481
Vaknown	D6\$37	5	2	0.4	Cervix	GCC_9:119
Unknown Unknown	D6537	5	4	0.8	Endocrine	CR 56:599
Unknown	D6937 D6S37	13	2	0.15	Esophageal	CR 5412996
Unknown	D6S37	13 25	4	0.31	Kidney	CR 51:820
Unknown	D6S37	23 29	9	0.36	Kidney	CR 51:5817
Unknown	D6937	10	1 4	0.03	Lung	CR 52:2478
Unknown	D6S37	13		0.4	Melanoma	CR 51:5449
Unknown	D6537	29	8 5	0.62	Ovary	BJC 67:551
Unknown	D6S37	14	***************************************	0.17	Ovary "	CR 51:5118
Onknown	D6537	30	3 11	0.21	Sarcoma	CR 52:2419
Unknown	D6S37	******************************	**************************************	0.37	Stomach	GCC 14:28
Unknown	D6537	29 11	2 1	0.07	Testis	0 9:2245 GCC 9:119
27	D6S446	24	11	0.09 0.46	Oterus	GCC 97119 GCC 15:223
Unknown	D6S132	15	11	0.46	Ovary	BJC 67:551
27	D6S281	27	5	0.73	Ovary Breast	BJC 71:290
27	D69281	39	13	0.19		GCC 15:223
the contract of the second sec	· · · · · · · · · · · · · · · · · · ·		and the state of t	······································	Ovary '	0 LL 13:443

Chromosome 6 - q Arm

27	Unknown	Unknown	22	2 .	0:09		
25.2-27	·····						
14-15	25.2-27	The same of the sa	***************************************			2000	
23.3-25.2 D53355 2	***						
21-23.3 D65357 20 2 0.1 Breast BJC 71:290	23.3-25.2				797970000000000000000000000000000000000	COTO CONTRACTOR CONTRA	
21-23 D65359 37 8	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		*********				
14-16	**************		***************************************				
15-21 D6548 3							BJC-715:2901
25.1 ER	CONTRACTOR STANDARDS CONTRACTOR		-		***************************************		
24 D6S135 9 5 0.56 Kidney CR 51:5817 21 D6S154 15 3 0.2 Kidney CR 51:5817 27 D69156 27 7 0.26 Kidney CR 51:5817 23 D6S164 11 1 0.09 Kidney CR 51:5817 D6XROWN D5S281-D6S311 22 4 0.18 Kidney PNAS 92:28 Unknown D6S281-D6S311 22 4 0.17 Kidney PNAS 92:28 Unknown D6S281-D6S311 6 1 0.17 Kidney PNAS 92:28 Unknown D6S281 0 0 Melanoma CR 54:7372 Unknown D6S29 4	****************						
21	**********						
27 D69156 27 7 0.26 Ktdney CR 51:5817							. CR 51:5817
23 D65164 11 1 0.09 Kidney CR.515817	***	Control of the Contro	************		***	*******************************	CR 51:5817
Display	***************************************			***************************************			CR:51:5817
DESCRIPTION DESCRIPTION		7.0700	***************************************		CHICAGO TO SECTION OF THE SECTION OF	Kidney	CR 51:5817
Unknown D65281-063311- D65278 6 1 0.17 Kidney PNAS 92:28 Unknown Unknown 20 15 0.75 Lung CR 54/2322 12.0-21 CGA 13 3 0.23 Melanoma CR 51:5449 Unknown D6929 4 0 0 Melanoma CR 51:5449 27 Unknown 130 4 0.03 Ovary IJC 52:575 Unknown Unknown 23 1 0.04 Ovary IJC 52:575 Unknown D65125 17 4 0.24 Ovary GC 55:245 27 D65193 10 1 0.1 Ovary GR 52:5815 27 D65193 11 1 0.48 Ovary GR 52:5815 27 D65193 23 11 0.48 Ovary GR 52:5815 Unknown D65225 26 0 0 Ovary GR 55:2169 Unknown D65366 1	OIIXIIOWII		22	22 24 7	0.18	Kidney 🚜	PNA5%92:2854
D6S278	Unknown	***************************************	6	1			
12.0-21 CGA	***************************************		0	1	0.17	Kidney	PNAS 92:2854
12.0-21 CGA	Unknown	-Unknown	20	15	0.75		
Onknown D6929 4 0 0 Melanoma CR 51:5449 27 Unknown 130 4 0.03 Ovary IJC 52:575 Unknown Onknown 23 1 0.04 Ovary IJC 52:575 13 ACTBP2 21 7 0.33 Ovary GC 57:551 27 D6S193 10 1 0.1 Ovary CR 52:5815 27 D6S193 11 1 0.09 Ovary CR 52:5815 27 D6S193 23 11 0.48 Ovary CR 52:5815 27 D6S193 23 11 0.48 Ovary CR 52:5815 Unknown D6S225 26 0 0 Ovary CR 55:2169 23.3-25.2 D69355 6 0 0 Ovary CR 55:2169 Unknown D6S265 13 0 0 Ovary CR 55:2169 Unknown D6S366 14 2	12.0-21	CGA	************				
27 Unknown 130 4 0.03 Ovary IJC 52:575 Unknown Unknown 23 1 0.04 Ovary IJC 52:575 13 ACTBP2 21 7 0.33 Ovary GO 55:245 Unknown D6S125 17 4 0.24 Ovary BJC 67:551 27 D6S193 10 1 0.1 Ovary CR 52:5815 27 D6S193 13 1 0.09 Ovary CR 52:5815 27 D6S193 23 11 0.48 Ovary CR 52:5815 27 D6S193 23 11 0.48 Ovary CR 55:2169 Unknown D6S225 26 0 0 Ovary CR 55:2169 23,3-25,2 D6S355 6 0 0 Ovary CR 55:2169 Unknown D6S366 14 2 0.14 Ovary CR 55:2169 Unknown B6S86 22 13	Unknown	D6929	*****************	FX-988-9-222-9-2-2-1	***************************************	A	Charles of the Contract of the
Unknown Unknown 23 1 B.04 Ovary IJC 52:575 13 ACTBP2 21 7 0.33 Ovary GO 55:245 Unknown D65125 17 4 0.24 Ovary BJC 67*551 27 D65193 10 1 0.1 Ovary CR 52:5815 27 D65193 11 1 0.09 Ovary CR 52:5815 27 D65193 23 11 0.48 Ovary CR 52:5815 27 D65193 23 11 0.48 Ovary CR 55:2169 Unknown D65225 26 0 0 Ovary CR 55:2169 23.3-25,2 D69355 6 0 0 Ovary CR 55:2169 Unknown D65366 14 2 0.14 Ovary CR 55:2169 Unknown D6586 22 13 0.59 Ovary BJC 67:551 Unknown HCG-A 8 4 <td>27</td> <td>Unknown</td> <td></td> <td></td> <td></td> <td></td> <td>•</td>	27	Unknown					•
13	Unknown	Unknown	********		CONTRACTOR OF THE PROPERTY OF THE PARTY OF T	THE RESERVE OF THE PARTY OF THE	
Onknown D6S125 17 4 Q:24 Ovary BJC 67:551 27 D6S193 10 1 0.1 Ovary CR 52:5815 27 D6S193 11 1 0.09 Ovary CR 52:5815 27 D6S193 23 11 0.48 Ovary CR 52:5815 Onknown D6S225 26 0 0 Ovary CR 55:2169 Unknown D6S225 13 2 0.15 Ovary CR 55:2169 23.3-25.2 D69355 6 0 0 Ovary CR 55:2169 Unknown D6S366 14 2 0.14 Ovary CR 55:2169 Unknown D6S366 19 1 0.05 Ovary CR 55:2169 Unknown D6S366 22 13 0.59 Ovary CR 55:2169 Unknown BCSA6 22 13 0.59 Ovary BJC 67:551 Unknown BCSA6 2	13		***************************************			*******************************	
27 D6S193 10 1 0.1 Ovary CR 52:5815 27 D6S193 11 1 0.09 Ovary CR 52:5815 27 D6S193 23 11 0.48 Ovary CR 52:5815 Unknown D6S225 26 0 0 Ovary CR 55:2169 Unknown D6S225 13 2 0.15 Ovary CR 55:2169 23.3-25.2 D69355 6 0 0 Ovary CR 55:2169 Unknown D6S366 14 2 0.14 Ovary CR 55:2169 Unknown D6S366 19 1 0.05 Ovary CR 55:2169 Unknown D6S86 22 13 0.59 Ovary BJC 67:551 Unknown BCSAA 8 4 0.5 Ovary BJC 67:551 Unknown IGF2R-D6S:251-249 17 3 0.18 Ovary CR 53:2393 Unknown MYB-DMDL-S0D2- DSS44	Unknown	CONTRACTOR OF CO	The same of the same of	***************************************	TO DESCRIPTION OF THE PARTY OF	77.90 99.90.90	THE PROPERTY OF THE PARTY OF TH
27 D6S193 11 1 0.09 Ovary CR 52:5815 27 D6S193 23 11 0.48 Ovary CR 52:5815 Unknown D6S225 26 0 0 Q Qvary CR 55:2169 Unknown D6S25 13 2 0.15 Ovary CR 55:2169 23.3-25.2 D6S355 6 0 0 O Ovary CR 55:2169 Unknown D6S366 14 2 0.14 Ovary CR 55:2169 Unknown D6S366 19 1 0.05 Ovary CR 55:2169 Unknown D6S86 22 13 0.59 Ovary CR 55:2169 Unknown D6S86 22 13 0.59 Ovary CR 55:2169 Unknown D6S86 21 13 0.59 Ovary CR 55:2169 Unknown D6S86 22 13 0.59 Ovary BJC 67:551 Unknown D6S86 22 13 0.59 Ovary BJC 67:551 Unknown IGF2R-D6S:251-249 17 3 0.18 Ovary BJC 67:551 Unknown MYB-DMDL-SOD2- 37 21 0.57 Ovary CR 53:2393 Unknown MYB-DMDL-SOD2- 37 21 0.57 Ovary CR 53:2393	***************************************	CONTRACTOR OF THE PROPERTY OF					***************************************
27 D6S193 23 11 0.48 Ovary CR 52:5815 Unknown D6S225 26 0 0 Ovary CR 55:2169 Unknown D6S225 13 2 0.15 Ovary CR 55:2169 23.3-25.2 D6S355 6 0 0 Ovary CR 55:2169 Unknown D6S366 14 2 0.14 Ovary CR 55:2169 Unknown D6S366 19 1 0.05 Ovary CR 55:2169 Unknown D6S86 22 13 0.59 Ovary BJC 67:551 Unknown HCG-A 8 4 0.5 Ovary BJC 67:551 Unknown IGF2R-D65:251-249 17 3 0.18 Ovary BJC 67:551 Unknown MYB-DMDL-SO02- 37 21 0.57 Ovary CR 53:2393 27 Unknown 3 0 0 Pancreas CR 54:2761 21/3 TNFB	27	The second secon			****	The state of the s	
Unknown D6S225 26 0 0 Ovary CR 55:2169 Unknown D6S225 13 2 0.15 Ovary CR 55:2169 23:33-25.2 D6S355 6 0 0 Ovary CR 55:2169 Unknown D6S366 14 2 0.14 Ovary CR 55:2169 Unknown D6S366 19 1 0.05 Ovary CR 55:2169 Unknown D6S86 22 13 0.59 Ovary BJC 67:551 Unknown BICG-A 8 4 0.5 Ovary BJC 67:551 Unknown IGF2R-D6S:251-249 17 3 0.18 Ovary BJC 72:133 Orknown MYB-DMDL-SOD2- 37 21 0.57 Ovary CR 53:2393 27 Unknown 3 0 0 Pancreas CR 54:2761 21/3 TNFB 13 2 0.15 Otary CR 54:2761	******		************				
Unknown D6S225 13 2 0.15 Ovary CR 55:2169 23:3=25.2 D6S355 6 0 0 Ovary CR 55:2169 Unknown D6S366 14 2 0.14 Ovary CR 55:2169 Unknown D6S366 19 1 0.05 Ovary CR 55:2169 Unknown D6S86 22 13 0.59 Ovary BJC 67:551 Unknown BICG-A 8 4 0.5 Ovary BJC 67:551 Unknown IGF2R-D6S:251-249 17 3 0.18 Ovary BJC 72:133 Orknown MYB-DMDL-SOD2- 37 21 0.57 Ovary CR 53:2393 27 Unknown 3 0 0 Pancreas CR 54:2761 21/3 TNFB 13 2 0.15 Otarus CR 54:2761	Unknown	***************************************	CONTRACTOR SOMEON CONTRACTOR	***	***************************************		
23.3-25.2 D69355 6 0 0 0 Ovary CR 55:2169 Unknown D68366 14 2 0.14 Ovary CR 55:2169 Unknown D68366 19 1 0.05 Ovary CR 55:2169 Unknown D6886 22 13 0.59 Ovary BJC 67:551 Unknown BCG-A 8 4 0.5 Ovary BJC 67:551 Unknown IGF2R-D65:251-249 17 3 0.18 Ovary BJC 72:133 Unknown MYB-DMDL-SOD2- 37 21 0.57 Ovary CR 53:2393 D6844 27 Unknown 3 0 0 Pancreas CR 54:2761 21.3 TNFB 13 2 0.15 Dterus CR 54:4294	······································	***************************************	••••••	***************************************	****		
Unknown D6S366 14 2 0.14 Ovary CR 55:2169 Unknown D6S366 19 1 0.05 Ovary CR 55:2169 Unknown D6S86 22 13 0.59 Ovary BJC 67:551 Unknown HCG-A 8 4 0.5 Ovary BJC 67:551 Unknown IGF2R-D6S:251-249 17 3 0.18 Ovary BJC 72:133 Unknown MYB-DMDL-SOD2- 37 21 0.57 Ovary CR 53:2393 27 Unknown 3 0 0 Pancreas CR 54:2761 21.3 TNFB 13 2 0.15 Oterus CR 54:4294	23.3-25.2	*****************************				PERSONAL PROPERTY AND ADDRESS OF THE PERSONAL PR	*************
Unknown D6S366 19 1 0.05 Ovary CR 55:2169 Unknown D6S86 22 13 0.59 Ovary BJC 67:551 Unknown HCG-A 8 4 0.5 Ovary BJC 67:551 Unknown IGF2R-D6S:251-249 17 3 0.18 Ovary BJC 72:133 Unknown MYB-DMDL-SOD2- 37 21 0.57 Ovary CR 53:2393 27 Unknown 3 0 0 Pancreas CR 54:2761 21/3 TNFB 13 2 0.15 Oterus CR 54:4294			***************************************		***************************************		
Unknown D6586 22 13 0.59 Ovary BJC 67:551 Unknown HCG-A 8 4 0.5 Ovary BJC 67:551 Unknown IGF2R-D65:251-249 17 3 0.18 Ovary BJC 72:133 Unknown MYB-DMDL-SOD2- 37 21 0.57 Ovary CR 53:2393 27 Unknown 3 0 0 Pancreas CR 54:2761 21:3 TNFH 13 2 0.15 Oterus CR 54:4294	************	THE RESERVE OF THE PARTY OF THE	**********	**************************************		and the second s	
Unknown HCG-A 8 4 0.5 Ovary BJC 67:551 Unknown IGF2R-D65:251-249 17 3 0.18 Ovary BJC 72:133 Unknown MYB-DMDL-SOD2- 37 21 0.57 Ovary CR 53:2393 27 Unknown 3 0 0 Pancreas CR 54:2761 21.3 TNFB 13 2 0.15 Oterus CR 54:4294	****************		**********************				***************************************
Unknown IGF2R-D65:251-249 17 3 0.18 Ovary BJC 72:133 Unknown MYB-DMDL-SOD2- 37 21 0.57 Ovary CR 53:2393 D6544 27 Unknown 3 0 0 Pancreas CR 54:2761 21.3 TNFB 13 2 0.15 Oterus CR 54:4294	ACRES TO THE STATE OF STREET	*************		***	CONTRACTOR CONTRACTOR OF THE PARTY OF THE PA	energy en generalis francis announce	
Unknown MYB-DMDL-SOD2- 37 21 0.57 Ovary CR 53:2393 D6544 27 Unknown 3 0 0 Pancreas CR 54:2761 21.3 TNFB 13 2 0.15 Oterus CR 54:4294	Accession of the Sales School	***************************************	******************************	**********			
D5544 27 Unknown 3 0 0 Pancreas CR 54:2761 21.3 TNFB 13 2 0.15 Oterus CR 54:4294	THE RESERVE OF THE PARTY OF THE	The first section of the section of	and the second s	PRODUCTOR	***************************************		
21.3 TNFB 13 2 0.15 Oterus CR 54:2761		No processor and processor of the second of	J1	- 21	0.57	Ovary	CR 53:2393
CIN UCBRUB LK 34:4294	*******************		~~~~~	****		Pancreas	CR 54:2761
3960 978 0.25	······································	INFE	000000000000000000000000000000000000000	***************************************	~~~~~ ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Oterus	CR-54:4294
	SUM		3960	978	0.25		

Chromosome 7 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
22	07821	36	5	0.14	Stomach	CR 51:2926
22	D7S21	19	1	0.05	Stomach	HG 92:244
22	D7S21	26	1	0.04	Testie	GCC: 13:249
Unknown	D7S517	6	0	0	Kidney	PNAS 92:2854
Unknown	-D7S517	-21	0	0	Kidney	PNAS 92:2854
Unknown	D7S370	18	3	0.17	Brain	CR 50:5784
Unknown	D79370	8	1	0.12	Breast	CR:50:7184
Unknown	D7S370	24	2	0.08	Cervix	CR 54:4481
Unknown	D7S370	24	5	0.21	Esophageal	CR 54:2996
Unknown	D75370	10	2	0,2	Kidney	CR 51:820
Unknown	D78370	10	0	- 0	Liver	CR 51:89
Unknown	D7S370	18	5	0.28	Lung	CR 52:2478
Unknown	พิสริสสัญ	26	4	0.15	Oyaxy	TUC 54 546
Unknown	D7S370	2	2	1	Pancreas	CR 54:2761
Unknown	075870	23		0.04	Testie	0-9;2245
Unknown	D7S370	20	2	0.1	Esophageal	GCC 10:177
Unknown	D75370	10	1 i	0.1	2000-2000-000-000-000-000-00-0	CR 51:2113
Unknown	D7S370	7	3	0.43	Ovarv	CR 51:5118
Unknown	D78370	17	2	0.12	Sarcoma	CR 52:2419
Unknown	D7S371	21	1	0.05	Breast	CR 53:4356
Unknown	D7S371	2	0	0	Ovarv	CR 51:5118
13.0-12	EGFR	8	1	0.12	Cervix	CR 49:3598
13.0-12	EGFR	4	0	0	Liver	PNAS 86:8852
11.2-12	EGFR	18	3	0.17	Ovary	BJC 69:429
11.2-12	EGFR	14	0	.0	Ovary	CR 49:1220
13.0-12	EGFR	5	1	0.2	Ovarv	CR 50:2724
Unknown	EGFR	11	0	0	Overy	CR 50:2724
13.0-12	EGFR	13	1	0.08	Prostate	G 11:530
Unknown	EGFR	10	0	0	Uterus	CR 51:5632
13.0-12	EGFR	16	2	0.12	Uterus	CR 54:4294
13.0-12	EGFR	16	2	0.12	Oterus	CR 54: 4294.
Unknown	D7S372	12	0	0	Brain	CR 49:6572
Unknown	D7S493	32	2	0.06	Cervix	CR 56:197
Unknown	D7S507	25	1	0.04	Cervix	CR 56:197
2.2-ter	Unknewn	25	1	0.03	Colon	BJC 59:750
Unknown	D7S481	22	16	0.73	Colon	CR 56:145
Unknown	D7S507	20	1	0.05	Endocrine	CR:56:599
Unknown	D7S481	21	0	0	Head&Neck	CR 54:4756
Unknown	D75481	22	4	0.18	Read&Neck	CR 54:4756
Unknown	D7S507	26	6	0.23	Head&Neck	CR 54:1152
pter-q22	Onknown	11	1	- 0.09	Liver	BJC 64:1083
pter-q22	Unknown	13	1	0.08	Liver	BJC 67:1007
Unknown	D75481	30	ī	0.03	Melanoma	CR 56:589
Unknown	D7S135	11	4	0.36	Ovary	CR 53:2393
prer-q22	Onknown	10	Ō	0.50	Pancies	EJC: 65: 809
2.2-ter	Unknown	10	0	0	Stomach	BJC 59:750
		_ •	-	5	- COMEC!	200 33.730

Chromosome 7 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
21.3-22.1	COLIA2	29	1	0.03	Breast	GCC 2:191
21.3-22.1	COLIA2	6	0	0	Cervix	CR 49:3598
21.3-22.1	COLIA2	12	0	0	Colon	N 331:273
21.3-22.1	COLIA2	15	1	0.07	Liver	JJCR 81:108
21.3-22.1	COLIA2	11	0	0	Liver	CCG 48:72
21.3-22.1	COLIA2	5	0	0	Neuroblaston	m CR 49:1095
21.3-22.1	COLIA2	10	2	0.2	Stomach	CR 52:3099
21.3-22.1	COLIA2	6	0	0	Uterus	CR 51:5632
Unknown	_D76527	21	4	0.19	Breast	PNAS 91:12155
Unknown	D7S527	8	1	0.12	Colon	CR 55:1347
Unknown	D78527	9	. 2	0.22	_Head&Neck	CR 55:1347
Unknown	D7S527	8	1	0.12	Prostate	CR 54:6370
Unknown	D75479	12	1	0.08	Breast	PNAS 91:12155
Unknown	D7S479	17	0	0	Endocrine	CR 56:599
Unknown	D79518	27	- 6	0.22	Breast	"PNAS 91:12155
Unknown	D7S518	8	0	0	Colon	CR 55:1347
Unknown	D78518	13	2	0.15		CR 55:1347
Unknown	D7S518	11	3	0.27	Prostate	CR 54:6370
Unknown	D79515	13	3	0.23	Breast	PNAS 91:12155
Unknown	D7S496	17	8	0.47	Breast	PNAS 91:12155
Unknown	D75496	13	4	0.31	Colon	CR 55:1347
Unknown	D7S496	10	1	0.1	Head&Neck	CR 55:1347
Unknown	D7S496	В	3	0.38	Prostate	CR 54:6370
22.3-31.2	D7S13	21	4	0.19	Breast	PNAS 91:12155
Unknown	D78523	22	12	0.55	Breast	PNAS 91:12155
Unknown	D7S523	9	4	0.44	Colon	CR 55:1347
Unknown	D78523	13	5	0.38	Head&Neck	CR 55:1347
Unknown	D7S523	7	2	0.29	Prostate	CR 54:6370
Unknown	D7918	7	3	0.43	Breast	PNAS 91:12155
Unknown	D7S486	15	5	0.33	Breast	PNAS 91:12155
Unknown	D7S486	18	9	0.5	Colon	CR:55:1347
Unknown	D7S486	10	3	0.3	Head&Neck	CR 55:1347
Unknown	D75486	6	2	0.33	Prostate	CR 54:6370
Unknown	D7S23	18	7	0.39	Breast	PNAS 91:12155
Unknown	D7823	11	1	0.09	Ovary	BJC 69:429
Unknown	D7523	15	2	0.13	Ovary	CR 53:2393
Unknown	D7923	20	3	0.15	Oterus	CR 54:4294
31	MET	31	1	0.03	Breast	CR 53:4356
31	MET	121		0.4	Breast	L_339:140
31	MET	221	8 4	0.38	Breast	GCC 12:304
31	MET	18	. 8	0.44	Breast	PNAS 91:12155
31 31	MET	24	2	0.08	Breast	GCC 2:191
***************************************	MET	15	Ō.	0	.Colon	CCG 48:167
31	MDR1-MET	12	0	0	Prostate	G 11:530
31	MET	9	3	0.33	Prostaté	,GCC: 11:119

Chromosome 7 - q Arm

31	MET	14	1	0.07	Sarcoma	CR 52:2419
31	MET	35	7	0.2	Stomach	IJC 59:597
31	MET	1	0	0	Testis	CCG 52:72
31	MET	1	0	0	Testis	CCG 52:72
31	MET	1	0	0	Testis	CCG 52:72
Unknown	D7S633	7	. 4	0.57	Colan	CR 55:1347
Unknown	D75633	6	2	0.33	Head&Neck	CR 55:1347
Unknown	D78633	7	3	0.43	Prostate	CR 54:6370
Unknown	D75677	9	6	0.67	Colon	CR 55:1347
Unknown	078677	10	4	0.4	Head&Neck	CR 55:1347
Unknown	D7S677	8	5	0.62	Prostate	CR 54:6370
Unknown	D75655	В	4	0.5	Colon	CR 55:1347
Unknown	D7S655	7	3 .	0.43	Head&Neck	CR 55:1347
Unknown	078655	14	6	0.43	Prostate	CR 54:6370
Unknown	D7S522	11	9	0.82	Breast	PNAS 91:12155
Unknovn	D78522	10	- 8	0,8	Colon	CR 55:1347
Unknown	D7S522	15	8	0.53	Head&Neck	CR 55:1347
Unknown	D7S522	. 6	5	0.83	Prostate	CR 54:6370
Unknown	D7S480	21	9	0.43	Breast	PNAS 91:12155
Unknown	D75480	27	4	0.15	Cervix	CR 56:197
Unknown	D7S480	16	7	0.44	Colon	CR 55:1347
Unknown	D75480	10	0	0.4	Head&Neck	CR 55:1347
Unknown	D7S480	11	3	0.27	Prostate	CR 54:6370
Unknown	D7S487	15	4	0.27	Ereast	PNAS 91:12155
Unknown	D75487	8	2	0.25	Colon	CR 55:1347
Unknown	D7S487	10	0	. 0	Head&Neck_	CR 55:1347
Unknown	D7S487	19	1	0.05	Leukemia	CR 55:5377
Unknown	D75487	. 9	1	0.12	Prostate	CR 54:6370
31	CFTR	9	2	0.22	Ovary	BJC 69:429
Unknown	D7S490	.14	5	0.36	Breast	PNAS 91:12155
Unknown	D7S490	10	4	0.4	Colon	CR 55:1347 ·
Unknown	D7,8490	12	4	0.33	Head&Neck	CR 55:1347
Unknown	D7S490	6	1	0.17	Prostate	CR 54:6370
31-32	078125	12	5	0.42	Breast	PNAS 91:12155
31-32	D7S125	15	2	0.13	Ovary	IJC 54:546
Unknown	D75504	22	6	0.27	Breast	PNAS 91:12155
Unknown	D7S514	10	1	0.1	Breast	PNAS 91:12155
Unknown	D7S500	19	3	0.16	Breast	PNAS 91:12155
Unknown	D75500	31	9	0.29	Cervix	CR 56:197
Unknown.	D75495	18		. 0	Breast	PNAS 91:12155_
Unknown	D7 S49 5	17	0	0	Head&Neck	CR 54:4756
Unknown	D7S495	20	1	0.05	Head&Neck	CR_54:4756
Unknown	D7S495	24	7	0.29	Head&Neck	CR 54:1152
Unknown	D78495	26	ı	0.04	Melanoma_	CR 56:589
Unknown	D7S498	18	2	0.11	Breast	PNAS 91:12155
Upknown	D7\$498	9	2	.0.22	Colon	CR 55:1347

Chromosome 7 - q Arm

Unknown D7549	Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 36 D75 36 D75 36 D75 36 D75 36 D75 36 D75 36 D75 36 D75 37 Unknown Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75	6483 9505 6396 6396 5396	19 1 1 5	1 (0 0 0	0.05	Breast	PNAS 91:12155
Unknown D73483 19	Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 36 D75 36 D75 36 D75 36 D75 36 D75 36 D75 36 D75 36 D75 37 Unknown Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75	3505 3396 3 396 3396	5	0 0	0.05		CONTRACTOR STATEMENT OF THE PARTY OF THE PAR
Unknown D78396 5	Unknown D75 Unknown D75	3396 3 396 3396	5	0	0	Propet	AND AND PROPERTY NAMED IN COLUMN TWO OF THE PARTY OF THE
Unknown D78396 22 3	Unknown D75	3 96 3396 3 39 6					PNAS 91:12155
Unknown D7S396 17	Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 36 D75 36 D75 36 D75 36 D75 36 D75 Unknown Unknown All 32—qter D75 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7	3396 33 9 6	22		0	Brain	CR 49:6572
Unknown D7S396 17	Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 36 D75 36 D75 36 D75 36 D75 36 D75 Unknown Unknown All 32—qter D75 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7	3396 33 9 6	and the second second	6 (0.27	Breast	PNAS 91:12155
Unknown D75396 17	Unknown D78 Unknown D78 Unknown D78 Unknown D78 Unknown D78 Unknown D78 Unknown D78 Unknown D78 36 D79 36 D79 36 D79 36 D79 36 D79 36 D79 Unknown Unknown All 32—qtex D71 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7	TO THE PERSON NAMED IN COLUMN 1	20			the state of the s	- properties and a respectation of the properties of
Unknown D78396 44 5 0.11 Esophageal GCC 10:177	Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 Unknown D75 36 D75 36 D75 36 D75 36 D75 36 D75 36 D75 36 D75 Unknown Unk Unknown All 32-qtex D71 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7	TO THE PERSON NAMED IN COLUMN 1		*****	COD/COC-16-1-170-000-000-000-000-000-000-000-000-0	ecoposoposocococomenomenos various	CONTRACTOR OF CO
Unknown D78396 23 5 0.25 Kidney CR.511820 Unknown D78396 28 3 0.11 Liver CR.51:89 Unknown D78396 34 5 0.13 Lunq CR.52:2478 Unknown D78396 19 4 0.21 Ovary CR.51:5118 Unknown D78396 19 4 0.21 Ovary CR.51:5118 Unknown D78396 19 0 0 Sarcoma CR.52:2419 36 D78550 6 0 0 Colon CR.55:1347 36 D78550 8 3 D.11 Esophagea LUC 69:1 36 D78550 8 1 0.12 Prostate CR.54:6370 36 D78550 8 1 0.12 Prostate CR.54:6370 36 D78550 8 1 0.12 Prostate CR.54:6370 36 D78550 8 1 0.12 Prostate CR.54:6370 36 D78550 8 1 0.12 Prostate CR.54:6370 36 D78550 8 1 0.12 Prostate CR.54:6370 36 D78550 8 1 0.12 Prostate CR.54:6370 36 D78550 8 1 0.12 Prostate CR.54:6370 36 D78550 8 1 0.12 Prostate CR.54:6370 36 D78550 8 1 0.12 Prostate CR.54:6370 37 Saction D7808 10 3 0.3 Cervix CR.54:4481 Unknown D7808 10 3 0.3 Cervix CR.54:4481 Unknown D7828 18 2 0.11 Cervix CR.54:4481 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG CCG 48:167 Unknown D78368 21 0 0 Colon CCG CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unknown D78368 21 0 0 Colon CCG 48:167 Unk	Unknown D78 Unknown D78 Unknown D79 Unknown D79 Unknown D79 36 D79 36 D79 36 D79 36 D79 36 D79 Unknown Unknown Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown Unknown Unknown Unknown				2000		Secretary and the second second second
Unknown D75396 28 3 0.11 Liver CR 51:89	Unknown D75 Unknown D75 Unknown D75 Unknown D75 36 D75 36 D75 36 D75 36 D75 36 D75 36 D75 Unknown Unknown All 32-qtex. D75 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7	396				200.00000 x 200.000000000000000000000000	
Unknown D75396 19 4 0.21 Ovary CR 52:2478 Unknown D75396 19 4 0.21 Ovary CR 51:5118 Unknown D75396 19 0 0 Sarcoma CR 52:2419 CR 52:2419 36 D75550 6 0 0 Colon CR 55:1347 36 D75550 6 0 0 0 Head&Neck CR 55:1347 36 D75550 8 1 0.12 Prostate CR 54:6370 D75550 8 1 0.12 Prostate CR 54:6370 D75550 8 1 0.12 Prostate CR 54:6370 D75550 8 1 0.12 Prostate CR 54:6370 D75550 8 1 0.12 Prostate CR 54:6370 D75550 8 1 0.12 Prostate CR 54:6370 D75550 B 1 0.12 Prostate CR 54:6370 D75550 B 1 0.12 Prostate CR 54:6370 D75550 D75500 D7555	Unknown D2 Unknown D7 Unknown 97 36 D7 36 D7 36 U7 36 U7 36 U7 36 U7 Unknown Unknown Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown Unknown Unknown Unknown	A	· · · · · · · · · · · · · · · · · · ·	THE RESIDENCE AND ADDRESS OF THE PARTY AND ADD	TAXABLE REPORTS		The state of the s
Unknown D7S396 19 4 0.21 Ovary CR 51:5118	Unknown D75 Unknown 975 36 D75 36 D75 36 D75 36 D75 36 D75 36 D75 Unknown Unk Unknown All 32-qter D75 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7 Unknown D7				***************************************		
Unknown	Unknown 973 36 D73 36 D73 36 D73 36 D73 36 D73 36 D73 40 D75 40 D	******************					
36 D78550 6 0 0 Colon CR 55:1347 36	36 D75 36 D75 36 D75 36 D75 36 D75 36 D75 Unknown Unk Unknown Al 32-qter. D75 Unknown D7 3.3-ter Unk Unknown D7 Unknown D7 Unknown D7 Unknown D7				*************		
36 D78550 28 3 D.11 Esophagea IUC 69:1	36 D7 36 D7 36 D7 36 D7 36 D7 Unknown Unk Unknown Al 32-qter D7 Unknown D7 3,3-ter Unk Unknown D7 Unknown D7 Unknown D7				THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TRANSPORT OF THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TRANSPORT NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TRANSPORT NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TRANSPORT NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TRANSPORT NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TRANSPORT NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TRANSPORT NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TRANSPORT N		
36	36 D79 36 D79 36 D79 36 D79 Unknown Unk Unknown Al 32-qter D79 Unknown D7 3,3-ter Unk Unknown D79 Unknown D79 Unknown D79			-			
36 D78550 B 1 0.12 Prostate CR 54:6370 36 D78550 8 1 0.12 Prostate CR 54:6370 Unknown Unknown 31 0 0 Brain CR 50:5784 Unknown ABP1 6 2 0.33 Breast PNAS 91:12155 32-qter D78228 18 2 0.11 Cervix GCC 9:119 Unknown D7896 10 3 0.3 Cervix GCC 9:119 3.3-ter Unknown 32 0 0 Colon BUC 59:750 Unknown D75368 21 0 0 Colon CCG 48:167 Unknown D7522 11 9 0 Endocrine N 328:524 Unknown D7522 1 9 0 Liver BUC 64:1083 36 Unknown 12 0 0 Liver BUC 67:1007 31.3-qter Unknown 19	36 D79 36 D79 Unknown Unk Unknown Al 32-qter D79 Unknown D7 3.3-ter Unk Unknown D79 Unknown D79 Unknown D79			· The residence of the second			CONTRACTOR CONTRACTOR
36	36 D73 Unknown Unk Unknown Al 32-qter D73 Unknown D7 3,3-ter Unk Unknown D7 Unknown D7 Unknown D7				****		
Unknown Unknown 31 0 0 Brain CR 50:5784 Unknown ABP1 6 2 0.33 Breast PNAS 91:12155 32-gter 078228 10 2 0:11 Cervix CR 54:4481 Unknown D7596 10 3 0.3 Cervix GCC 9:119 3.3-tex Unknown 32 0 0 Colon BUC 59:750 Unknown D75368 21 0 0 Colon CCG 48:167 Unknown Unknown 10 0 0 Endocrine N 328:524 Unknown Unknown 10 0 0 Liver BJC 64:1083 36 Unknown 12 0 0 Liver BJC 67:1007 31.3-qter Unknown 7 1 0.14 Pancreas BJC 65:809 36 Unknown 19 2 0.11 Prostate CSurveys 11:15 Unknown 19 2 </td <td>Unknown Unk Unknown Al 32-qter 07: Unknown D7 3.3-ter Unk Unknown D7: Unknown D7: Unknown Unk</td> <td>STOREGIST STANDARD STANDARD</td> <td>or president property and the second</td> <td>ALL AND ALL PROPERTY AND ADDRESS OF THE PARTY OF THE PART</td> <td>*****</td> <td></td> <td>martine, is any other properties of the parties of</td>	Unknown Unk Unknown Al 32-qter 07: Unknown D7 3.3-ter Unk Unknown D7: Unknown D7: Unknown Unk	STOREGIST STANDARD STANDARD	or president property and the second	ALL AND ALL PROPERTY AND ADDRESS OF THE PARTY OF THE PART	*****		martine, is any other properties of the parties of
Unknown ABP1 6 2 0.33 Breast PNAS 91:12155 32-qter 07\$228 18 2 0:11 Cervix CR 54:4481 Unknown D7\$96 10 3 0.3 Cervix GCC 9:119 3.3-ter Unknown 32 9 0 Colon BUC 59:750 Unknown D7\$368 21 0 0 Colon CCG 48:167 Unknown D7\$22 11 0 0 Endocrine N 328:324 Unknown Unknown 10 0 0 Liver BJC 64:1083 36 Unknown 12 0 0 Liver BJC 67:1007 31.3-qter Unknown 7 1 0.14 Pancreas BJC 65:809 31.3-qter Unknown 19 2 0.11 Prostate CSurveys 11:15 Unknown Unknown 19 2 0.11 Prostate PNAS 87:8731 3.3-ter Unknown <td>Unknown Al 32-qter. 07; Unknown D7 3.3-ter Unk Unknown D7; Unknown D7; Unknown Unk</td> <td></td> <td></td> <td>***************************************</td> <td></td> <td>******************************</td> <td>************************</td>	Unknown Al 32-qter. 07; Unknown D7 3.3-ter Unk Unknown D7; Unknown D7; Unknown Unk			***************************************		******************************	************************
32-qter D78228 18 2	32-qter 07: Unknown D7 3.3-tex Unk Unknown D7: Unknown D7 Unknown Unk	TITLE CITATION IS EMPOSED TO	O'T COMMANDE A SECOND TO THE PERSON TO THE P	CAN CONTRACTOR OF STATE OF STA	CONT. TOP A COLOR WATER OF THE COLOR	TO THE PERSON NAMED AND POST OF THE PERSON NAMED AND PARTY OF THE	
Unknown D7596 10 3 0.3 Cervix GCC 9:119 3.3=tex Unknown J2 Q 0 Colon BUC 59:750 Unknown D75368 21 0 0 Colon CCG 48:167 Unknown D7522 11 0 0 Endocrine N 328:524 Unknown Unknown 10 0 0 Liver BUC 64:1083 36 Unknown 12 0 0 Liver BUC 67:1007 31.3-qter Unknown 7 1 0.14 Pancreas BUC 65:809 36 Unknown 4 0 0 Pancreas BUC 65:809 31.3-qter Unknown 19 2 0.11 Prostate CR 54:2761 31.3-qter Unknown 19 2 0.11 Prostate CSurveys 11:15 Unknown Unknown 9 0 0 Stomach BUC 59:597 Unknown D7522	Unknown D7 3.3-tex Unk Unknown D7 Unknown D7 Unknown Unk		-	******************************	*****	******************************	
3.3-tex	3.3-tex Unk Unknown D7: Unknown D7 Unknown Unk	- L. Y. o. C. Charles Street of the Philips Str. Y		T. Actor and A. Strategic	AND THE PERSON NAMED IN COLUMN 2	T 1-1 1 1 1 1 1 1	TO SECTION AND ASSESSMENT ASSESSMENT AND ASSESSMENT AND ASSESSMENT ASSESSMENT AND ASSESSMENT ASS
Unknown D75368 21 0 0 Colon CCG 48:167 Unknown D7522 II 0 0 Endocrine N 328:524 Unknown Unknown 10 0 0 Liver BJC 64:1083 36 Unknown 12 0 0 Liver BJC 65:809 31.3-qter Unknown 7 1 0.14 Pancreas BJC 65:809 35 Unknown 4 0 0 Pancreas BJC 65:809 31.3-qter Unknown 19 2 0.11 Prostate CR 54:2761 31.3-qter Unknown 19 2 0.11 Prostate CSurveys 11:15 Unknown Unknown 19 2 0.11 Prostate PNAS 87:8731 3.3-ter Unknown 9 0 0 Stomach BJC 59:597 Unknown D7522 47 11 0.23 Stomach CR 51:2926 Unknown D7564 </td <td>Unknown D7: Unknown D7 Unknown Unk</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	Unknown D7: Unknown D7 Unknown Unk						
Unknown D7522 11 0 0 Endocrine N 328:524 Unknown Unknown 10 0 0 Liver BJC 64:1083 36 Unknown 12 0 0 Liver BJC 67:1007 31.3-qter Unknown 7 1 0.14 Pancreas BJC 65:809 36 Unknown 4 0 0 Pancreas CR 54:2761 31.3-qter Unknown 19 2 0.11 Prostate CSurveys 11:15 Unknown Unknown 19 2 0.11 Prostate PNAS 87:8731 3.3-ter Unknown 9 0 0 Stomach BJC 59:750 Unknown D7522 47 11 0.23 Stomach IJC 59:597 Unknown D7522 41 10 0.24 Stomach IJC 59:597 Unknown D7564 16 0 0 Stomach IJC 59:597 Unknown D7595 <td>Unknown D7 Unknown Unk</td> <td></td> <td></td> <td>***************************************</td> <td>********</td> <td>Contract to the second section of the section of the section</td> <td></td>	Unknown D7 Unknown Unk			***************************************	********	Contract to the second section of the section of the section	
Unknown Unknown 10 0 0 Liver BJC 64:1083 36 Unknown 12 0 0 Liver BJC 67:1007 31.3-qter Unknown 7 1 0.14 Pancreas BJC 65:809 36 Unknown 4 0 0 Pancreas CR 54(2761 31.3-qter Unknown 19 2 0.11 Prostate CSurveys 11:15 Unknown Unknown 19 2 0.11 Prostate PNAS 87:8731 3.3-ter Unknown 9 0 0 Stomach BJC 59:750 Unknown D7522 47 11 0.23 Stomach IJC 59:597 Unknown D7522 41 10 0.24 Stomach CR 51:2926 Unknown D7564 16 0 0 Stomach IJC 59:597 Unknown D7595 30 13 0.43 Stomach IJC 59:597 Unknown D7522<	Unknown Unk			0		*****	
36 Unknown 12 0 0 Liver BJC 67:1007 31.3-qter Unknown 7 1 0.14 Pancreas BJC 65:809 36 Unknown 4 0 0 Pancreas CR:54:2761 31.3-qter Unknown 19 2 0.11 Prostate CSurveys 11:15 Unknown Unknown 19 2 0.11 Prostate PNAS 87:8751 3.3-ter Unknown 9 0 0 Stomach BJC 59:750 Unknown D7522 47 11 0.23 Stomach IJC 59:597 Unknown D7522 41 10 0.24 Stomach IJC 59:597 Unknown D7564 16 0 0 Stomach IJC 59:597 Unknown D7595 30 13 0.43 Stomach IJC 59:597 Unknown D7522 22 2 0.09 Testis GCC 13:249 32-qter D7522		T. L. DE STATE OF STA	CHARLES AND AND ADDRESS OF THE PARTY OF THE	***************************************	THE PERSON NAMED IN COLUMN	The second secon	
31.3-qter Unknown 7 1 0.14 Pancreas BJC 65:809 36 Unknown 4 0 0 Pancreas CR 54(276) 31.3-qter Unknown 19 2 0.11 Prostate CSurveys 11:15 Unknown Unknown 19 2 0.11 Prostate PNAS 87:8731 3.3-ter Unknown 9 0 0 Stomach BJC 59:750 Unknown D7522 47 11 0.23 Stomach IJC 59:597 Unknown D7522 41 10 0.24 Stomach CR 51:2926 Unknown D7563 35 8 0.23 Stomach IJC 59:597 Unknown D7564 16 0 0 Stomach IJC 59:597 Unknown D7595 30 13 0.43 Stomach IJC 59:597 Unknown D7522 22 2 0.09 Testis GCC 13:249 32-qter <t< td=""><td></td><td>********</td><td></td><td></td><td></td><td>***</td><td></td></t<>		********				***	
36 Unknown 4 0 0 Pancress CR 54:2761 31.3-qter Unknown 19 2 0.11 Prostate CSurveys 11:15 Unknown Unknown 19 2 0.11 Prostate PNAS 87:8751 3.3-ter Unknown 9 0 0 Stomach BJC 59:750 Unknown D7522 47 11 0.23 Stomach IJC 59:597 Unknown D7522 41 10 0.24 Stomach CR 51:2926 Unknown D7563 35 8 0.23 Stomach IJC 59:597 Unknown D7564 16 0 0 Stomach IJC 59:597 Unknown D7595 30 13 0.43 Stomach TJC 59:597 Unknown D7522 22 2 0.09 Testis GCC 13:249 32-qter D75228 23 2 0.09 Testis 0.9:2245	"> destruction of the contract country to the contract of the	the second secon			the second secon	*	interest and in the contract of the contract o
31.3-qter Unknown 19 2 0.11 Prostate PNAS 87:8751	- Commission of the Commission	***************************************			WANTAN IN AN AN AN AN AN AN AN AN AN AN AN AN AN	######################################	CONTRACTOR OF THE PROPERTY OF
Unknown Unknown 19 2 0:11 Prostate PNAS 87:8751 3.3-ter Unknown 9 0 0 Stomach BJC 59:750 Unknown D7522 47 11 0:23 Stomach IJC 59:597 Unknown D7522 41 10 0:24 Stomach CR 51:2926 Unknown D7563 35 8 0:23 Stomach IJC 59:597 Unknown D7564 16 0 0 Stomach IJC 59:597 Unknown D7595 30 13 0:43 Stomach TJC 59:597 Unknown D7522 22 2 0:09 Testis GCC 13:249 32-qter D75228 23 2 0:09 Testis 0:9:2245				CONTRACTOR CONTRACTOR	CHILLIAN STATES OF THE PARTY OF	Service and the service and th	Office of the stat
3.3-ter Unknown 9 0 0 Stomach BJC 59:750 Unknown D7522 47 11 0.23 Stomach LJC 59:597 Unknown D7522 41 10 0.24 Stomach CR 51:2926 Unknown D7563 35 8 0.23 Stomach LJC 59:597 Unknown D7564 16 0 0 Stomach LJC 59:597 Unknown D7595 30 13 0.43 Stomach TJC 59:597 Unknown D7522 22 2 0.09 Testis GCC 13:249 32-qter D73228 23 2 0.09 Testis 0.9:2245	******************************					***************************************	MANAGEMENT TO THE PROPERTY OF
Unknown D7522 47 11 0.23 Stomach LJC 59:597 Unknown D7522 41 10 0.24 Stomach CR 51:2926 Unknown D7563 35 8 0.23 Stomach LJC 59:597 Unknown D7564 16 0 0 Stomach LJC 59:597 Unknown D7595 30 13 0.43 Stomach TJC 59:597 Unknown D7522 22 2 0.09 Testis GCC 13:249 32-qter D79228 23 2 0.09 Testis 0.9:2245		CONTRACTOR SERVICES NO.	***************************************	27.1.003.04.04.04.000.05.00.000.000.000.000.000.	NAMES - CONTROL OF THE OWNER, OF THE PARTY O	***************************************	the property of the control of the c
Unknown D7S22 41 10 0.24 Stomach CR 51:2926 Unknown D7S63 35 B 0.23 Stomach IJC 59:597 Unknown D7S64 16 0 0 Stomach IJC 59:597 Unknown D7S95 30 13 0.43 Stomach IJC 59:597 Unknown D7S22 22 2 0.09 Testis GCC 13:249 32-qter D7S228 23 2 0.09 Testis 0.9:2245	**************************************				.	Carron or consequence assessment and the section of	The second secon
Unknown B7863 35 8 0:23 Stomach IJC 59:597 Unknown D7864 16 0 0 Stomach IJC 59:597 Unknown D7895 30 13 0:43 Stomach IJC 59:597 Unknown D7822 22 2 0:09 Testis GCC 13:249 32-qter D78228 23 2 0:09 Testis 0:9:2245	to a series of a description of provide description of provide	PACE TANDAMENT AND ADMINISTRATION OF THE PACE TO SECURITION OF THE PAC	SECTION AND DESCRIPTION OF A SECTION AS	TO CHARLES AND ADDITION OF COMPANY AND ASSESSMENT OF COMPANY AND ADDITION OF C		* * * * * * * * * * * * * * * * * * * *	175 000-100 0 1150 100 100 110 110 110 110 110 1
Unknown D7S64 16 0 0 Stomach IJC 59:597 Unknown D7595 30 13 0.43 Stomach TJC 59:597 Unknown D7S22 22 2 0.09 Testis GCC 13:249 32-qter D73228 23 2 0.09 Testis 0.9:2245	ALTERNATION COMMISSION					annon 3 100 men 200 emperator 300 200 200 200 200 200 200 200 200 200	
Unknown D7595 30 13 0.43 Stomach TJC 59:597 Unknown D7522 22 2 0.09 Testis GCC 13:249 32-qter D73228 23 2 0.09 Testis 0.9:2245	7-19-10-1-10-1-10-10-10-10-10-10-10-10-10-10	~~ ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		8		Stomach	D 220 C20 C100000000000000000000000000000
Unknown D7522 22 2 0.09 Testis GCC 13:249 32-qter D75228 23 2 0.09 Testis 0.9:2245	Unknown D7	7564		0	0	Stomach	
32-qter D79228 23 2 0.09 Testis D.9:2245	Unknown D	1595	30	13	0.43	Stomach	IJC 59:597
12 million and 1						Testis	
	32-qterD7	9228	23	2	0.09	Testis	0.9:2245
Unknown TCBR 3 0 0 Testis CCG 52:72						Testis	
Unknown TCBR 3 0 Testis CCG 52:72	Unknown T	CBR	3	0	0	Testis	CCG 52:72
Unknown TCBR 2 0 0 Testis CCG 52:72	Unknown T					Testis	
11_23 D78440 19 1 D:05 Overus: CR:54:4294	D7		19	1	0:05	Oterus	CR 54:4294
Unknown D7S96 16 3 0.19 Uterus GCC 9:119	Unknown D	8440		_	0.19	Uterus	GCC 9:119
SUM 2325 517 0.22	SUM	7896					**************************************

WO 98/41648

PCT/US98/05419

67 / 214

Chromosome 7 - p Arm

SUM 747 67 0.12

Chromosome 8 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
21	08917	21	7	0.33	Breast	CR 53:4356
21	D8517	3	1	0.33	Breast	CR 53:3804
21	D8S17	9	-1	0.11	Ovary	IJC 54:546
Unknown	D85264	30	6	0.2	Cervix	CR 56:197
Onknown	D85262	5	2	0.4	Kidney	GCC 12:76
Unknown	D8S262	15	2	0.13	Leukemia	CR 55:5377
Unknown	D85262	18	9	0.5	Prostate	The second of th
23	D8S201	9	5	0.56	Colon	CR 54:6061
23″	D86201	28	6	0.21	CONTRACTOR OF THE PARTY OF THE	AJP 144:1
23	D8S201	15	8		Prostate	0.11:2121
23	D8S201	722		0.53	Prostate	AJP 144:1
23			3,	0,14	Prostate	CR 53:3869
23 23	D8S201	3	1	0.33	Sarcoma	AJP 144:1
	D857	11	5	0.45	Colon	GCC,10:1
23	D8S7	18	6	0.33	Esophageal	CR 54:2996
23	D897	10	4	0.4	Ovary:	CR 53:2393
23	D8S7	8	3	0.38	Prostate	GCC 3:215
23	D857	- 6	3	0.5	Prostate	G 11:530
23	D857	10	1	0.1	Sarcoma	CR 52:2419
Unknown	D8S277	18	Ō	0	Endocrine	CR 56:599
Unknown	D85277	26	11	0.42	Prostate	CR 54:6061
23.12	D8S337	18	5	0.28	Colon	CR 53:1172
23.12	D8S337	15	7	0.47	Liver	GCC 7:152
23.12	D85337	3	0	٥	Lung	GCC 8:75
23.12	D8S337	14	6	0.43	Prostate	GCC 13:168
23.12	D85336	39	10	0.26	Colon	CR 53:1172
23.12	D8S336	48	18	0.38	Liver	GCC 7:152
23.12	D8S336	7	3	0.43	Lung	GCC 8:75
21.3-22	D8S335	53	18	0.34	Colon	CR 53:1172
21.3-22	D85335	30	15	0.5	Colon	GCC 10:7
21.3-22	D8S335	46	17	0.37	Liver	GCC 7:152
21.3-22	D8S335	18		*****		· · · · · · · · · · · · · · · · · · ·
21.3-22	D8S335		Control of the Contro	0.22	Liver	GCC 10:7
21.3-22	D8S335	27 5	12	0.44	Lung	GCC 10:7
Unknown			1	0.2	Lung	GCC 7:85
WESTERNIE COTTOCCCO CONTROL CO	D8S265	22	5	0.23	Cervix	CR 56:197
Unknown 22	D8S265	22	11	0.5	Prostate	CR 54:6061
	CTSB	33	14	0.42	Colon	CR 53:1172
22	CTSB	23		0.3	Liver	GCC 7:152
11.212	Unknown	33	10	0.3	Colon	CR 52:5368
11.212	Unknown	34	В	0.24	Colon	CR_53:1172
11.212	Unknown	34	0	0	Liver	GCC 7:152
11.212	Vaknown	. 12	0	0	Lung	GCC 7:85
Unknown	D8S254	13	4	0.31	Breast	CR 55:4995
Unknown	D8S261	16	1	0.06	Head&Neck	CR 54:4756
Unknown	D8S261	18	1	0.06	Head&Neck	CR 54:4756
Onknown	D8S261	20	8	0.4	Read&Neck	CR 54:1152
Unknown	D8S261	6	3	0.5	Kidney	GCC 12:76
				-		

Chromosome 8 - p Arm

Unknown	D89261	24	. 3	0.12	Melanoma	CR 56:589
Unknown	D8S261	31	17	0.55	Prostate	CR 54:6061
22-prer	D8S153	44	- 19	0.43	Colon	CR 53:1172
22-pter	D8S163	31	14	0.45	Liver	GCC 7:152
22-pter	D89163	14	3	0.21	Lung	GCC18:75
22-pter	D8S163	1	0	0	Pancreas	CR 54:2761
22-pter	D85163	23	14	0.61	Prostate	CR 53:3869
22-pTER	D85163	18	9	0.5	Prostate	GCC 13:168
21.3-22	CI8-1344	71	25	0.35	Colon	GCC 10:7
21.3-22	CI8-I344	40	10	0.25	Liver	GCC 10:7
21.3-22	CI8-1344	30	- 8	0.27	Lung	GCC 10:7
21.3-22	CI8-2195	35	15	0.43	Colon	GCC 10:7
21,3-22	C18-2195	32	7	0.22	Liver	GCC 10:7
21.3-22	CI8-2195	20	6	0.3	Lung	GCC 10:7
21,3-22	C18-2014	24	7	0.29	Colon	GCC 10:7
21.3-22	CI8-2014	6	2	0.33	Liver	GCC 10:7
21.3-22	CI8-2014	17	7	0.41	Long	GCC 10:7
21.3-22	CI8-2014	8	3	0.38	Prostate	GCC 13:168
21.3-22	D85233	21	10	0.48	Colon	GCC 10:7
21.3-22	D8S233	24	11	0.46	Colon	CR 53:1172
21,3-22	D89233	28	12	0.43	Liver	GCC 7:152
21.3-22	D8S233	14	5	0.36	Liver	GCC 10:7
21.3-22	D8S233	9	2	0.22	Lung	GCC 8:75
21.3-22	D8S233	7	3	0.43	Lung	GCC 10:7
Unknown	MSR	56	5	0.09	Breast	CR 52:5368
21.3-22	MSR	74	27	0.36	Colon	GCC 10:7
Unknown	MSR	26	12	0.46	Colon	CR 52:5368
22	MSR	74	28	0.38	Colon	CR 53:1172
Unknown	MSR	27	2	0.07	Kidney	CR 52:5368
Unknown 22	MSR MSR	33	14	0.42	Liver	JJCR 84:893
21.3-22	MSR		37	0.43	Liver	GCC 7:152
Unknown	MSR	35	10 14	0.19	Liver	GCC 10:7
Unknown	MSR	21	9	0.4	Lung	CR 52:5368
21.3-22	MSR	38	16	0.43	Lung	GCC 8:75
Unknown	MSR	12	4	0.42	Lung	GCC 10:7
21.3-22	MSR	29	18	0.33	Ovary	CR 52:5368
22	MSR	29	20	0.62	Prostate	GCC 13:168
Onknown	MSR	18	4	0.69	Prostate	CR 53:3869 CR 52:5368
21.3-22	Unknown	33	16	0.22	Stomach	***************************************
Z1.3-22	Unknown	9	3	0.48	Colon	GCC 10:7
21.3-22	Unknown	20	12	0.33 0.6	Liver	GCC 10:7
21.3-22	Unknown	18	11	0.61	Lung	GCC 13:168
21.3-22	Unknown	21	9	0.43	Prostate Colon	GCC 10:7
21.3-22	Unknown	6	2	0.43	× Liver	GCC 10:7
21.3-22	Unknown	22	15	0.68	######################################	······································
22	O. A. I.OWI.	44	دد	0.55	Lung	GCC 10:7

Chromosome 8 - p Arm

21.3-22	Unknown	47	19	0.45	Colon	GCC 10:7
21.3-22	Unknown	33	10	0.3	Liver	GCC 10:7
21.3-22	Unknown	21	10	0.48	Lung	GCC 10:7
21.3-22	Unknown	15	8	0.53	Prostate	GCC 13:168
21.3-22	Unknown	48	-14	0.29	Colon	GCC 10,7
21.3-22	Unknown	39	9	0.23	Liver	GCC 10:7
21.3-22	Unknown	22	7	0.32	Lung	GCC 10:7
21.3-22	Unknown	15	8	0.53	Prostate	GCC 13:168
21.3-22	Unknown	49	22	0.45	Colon	GCC 10:7
21.3-22	Unknown	40	9	0.23	Liver	GCC 10:7
21.3-22	Unknown	23	7	0.3	Lung	GCC 10:7
21.3-22	Unknown	15	8	0.53	Prostate	GCC 13:168
21.3-22	Unknown	51	31	0.61	Colon	GCC 10;7
21.3-22	Unknown	54	16	0.3	Liver	GCC 10:7
21.3-22	Unknown	2.0		- 0.21	Lung	GCC 10:7:
21.3-22	Unknown	20	8	0.4	Colon	GCC 10:7
21,3-22	Unknown	25	.7	0.28	Liver	GCC 10:7:1
21.3-22	Unknown	17	4	0.24	Lung	GCC 10:7
21	Unknown	1	0,	0	Pancreas .	CR 54:2761
22	LPL	10	4	0.4	Colon	GCC 11:195
22	LPL	13	2	0.15	Colon	AJP 144:1
22	LPL	32	4	0.12	Colon	GCC 10:1
22	LPL	21	3	0.14	Colon	CR 53:1172
22	LPL	47	10	0.21	Colon	BJC 70:18
22	LPL	17	. 4	0.24	Leukemia	B.83:3449
22	LPL	38	19	0.5	Liver	GCC 7:152
22	LPL	6	4	0.67	Lung	CR 55:28
22 22	LPL	7	3	0.43	Lung	GCC 8:75
	LPL	19	8	0.42	Prostate	AJP 144:1
22 	LPL LPL	13	5	0.38	Prostate	GCC 13:278
22	LPL	***************	6	0.86	Prostate	GCC_3:215
22	LPL	32 24	15 11	0.47	Prostate	CR 53:3869
p22	LPL-G214-15	***********		0.46	Prostate	0 11:2121
22	LPL LPL	29	14	0.48	Prostate	CR 54:6061
22	LPL	2 19	0	0	Sarcoma	AJP 144:1
Unknown	D89258	memerana con comencia	2 3	0.11	Uterus	CR 54:4294
Unknown	D85282	16		0.19	Breast	CR 55:4995
Unknown	D8S298	27 30	13 18	0.48	Prostate	CR 54:6061 CR 54:6061
21.3	D8S232	59	17	0.6 0.29	Prostate	CR 53:1172
21.3	D89232	40	13	0.29	Colon Liver	GCC 7:152
21.3	D8S232	19	7	0.37	Lung	GCC 7:132
21.3	D85334	47	16	0.34	Colon	CR 53:1172
21.3-22	D8S334	49	18	0.37	Colon	GCC 10:7
21.3-22	D85334	37	8	0.22	Liver	GCC 10:7
21.3	D8S334	39	15	0.38	Liver	GCC 7:152

Chromosome 8 - p Arm

21.3 D8S334 6 2 0.33 Lung GCC 7:8 21:3 D8S334 16 9 0.56 Prostate GCC 13 21-23 EGR3 28 14 0.5 Colon CR 53:1	1172 157 1172 1172 152 152 1119 121 6061
21:3 D8S334 16 9 0.56 Prostate GCC 13 21-23 EGR3 28 14 0.5 Colon CR 53:: 21-23 EGR3 33 12 0.36 Liver GCC 79: 21.23 CI8-586 25 7 0.28 Colon CR 53:: 21.23 CI8-586 20 9 0.45 Liver GCC 7:: 21 D8S133 10 5 0.5 Prostate GCC 11 21 D8S133 27 7 0.26 Prostate 0.11:2 21 D8S133 29 16 0.55 Prostate CR 54:: 21.23 D8S220 50 18 0.36 Colon CR 53::	1172 157 1172 1172 152 152 1119 121 6061
21-23 EGR3 28 14 0.5 Colon CR 53:: 21-23 EGR3 33 12 0.36 Liver GCC 7:: 21.23 CI8-586 25 7 0.28 Colon CR 53:: 21.23 CI8-586 20 9 0.45 Liver GCC 7:: 21 D8S133 10 5 0.5 Prostate GCC 11 21 D8S133 27 7 0.26 Prostate 0.11:2 21 D8S133 29 16 0.55 Prostate CR 54:: 21.23 D8S220 50 18 0.36 Colon CR 53::	1172 152 1172 152 :119 :119 121 6061
Z1-23 EGR3 33 T2 0.36 Liver GCC 7:0 21.23 CI8-586 25 7 0.28 Colon CR 53:1 21.23 CI8-586 20 9 0.45 Liver GCC 7:0 21 D8S133 10 5 0.5 Prostate GCC 11 21 D8S133 27 7 0.26 Prostate 0.11:2 21 D8S133 29 16 0.55 Prostate CR 54:0 21.23 D8S220 50 18 0.36 Colon CR 53:0	157 1172 152 :119 121 6061
21.23 CI8-586 25 7 0.28 Colon CR 53:1 21.23 CIB-586 20 9 0.45 Liver GCC 7:3 21 D8S133 10 5 0.5 Prostate GCC 1:3 21 D89133 27 7 0.26 Prostate 0.11:2 21 D8S133 29 16 0.55 Prostate CR 54:4 21.23 D8S220 50 18 0.36 Colon CR 53:2	1172 152 :119 121 6061
21.23 CIB-586 20 9 0.45 Liver GCC 7. 21 D8S133 10 5 0.5 Prostate GCC 11 21 D89133 27 7 0.26 Prostate 0.11:2 21 D8S133 29 16 0.55 Prostate CR 54: 21.23 D8S220 50 18 0.36 Colon CR 53:	152 :119 121 6061
21 D8S133 10 5 0.5 Prostate GCC 11 21 D89133 27 7 0.26 Prostate 0.11:2 21 D8S133 29 16 0.55 Prostate CR 54:0 21.2-3 D8S220 50 18 0.36 Colon CR 53:0 21.2-3 D8S220 50 18 0.36 Colon CR 53:0	:119 121 6061
21 D89133 27 7 0.26 Prostate GCC 11 21 D85133 29 16 0.55 Prostate CR 54:0 21.2-3 D85220 50 18 0.36 Colon CR 53:0 21.2-3 D85220 50 18 0.36 Colon CR 53:0	121 6061
21 DBS133 29 16 0.55 Prostate CR 54:0 21.2-3 DBS220 50 18 0.36 Colon CR 53:	6061
21.2-3 D8S220 50 18 0.36 Colon CR 53:	***************************************
21 2- 3 D00220	11/2
21.23 D89220 43 16 D.37 Liver CR 52:	
21.23 D8S220 50 17 0.34 Liver GCC 7:1	
21.23 D85220 17 4 0:24 Lung GCC 7:	7750
21.23 D8S220 18 6 0.33 Prostate GCC 13:	
21.2-3 D89220 27 16 D.59 Prostate CR.53:	***************************************
Unknown SFTP2 40 11 0.28 Colon GCC 10:	
Unknown D8S136 20 7 0.35 Breast CR 55:	~~~
Unknown D85136 11 6 0.55 Colon GCC 11	**********
	4:1
Unknown D8S136 28 16 0.57 Prostate CR 54:0	
21.12 D85221 53 14 0.26 Colon CR 53:	
21.12 D85221 41 10 0.24 Liver 'GCC 7:	***********
21,1-2 D85221 10 0 0 Lung GCC 7;8	85
21 NEFL 15 1 0.07 Brain CR 50:5	5784
21 NEFL 2 1 0.5 Breast CR 53:	3804
21 NEFL 22 3 0.14 Cervix CR 54:4	4481
21 NEFL 35 11 0.31 Colon GCC 10	.1
21 NEFL 8 4 0.5 Colon GCC 11	:195
21 NEFL 50 22 0:44 Colon CR 53:	1172
21 NEFL 47 19 0.4 Liver GCC 7::	152
9,30 tung GCC [1]	85
2 0.33 Prostate CR 53:	
0.00 Flostace aco.3:	
0.42 Prostate GCC 13	con concess to reconstant.
21 USCACE UILLA	***********
0.16 lestis 09:224	
Unknown Doctor	
29 U.34 Colon BJC /U:	**********
Unknown Prostate AMP 14	
TO U./ Prostate CR 54:0	Authorities de la contraction de
Unknown	***************************************
0.39 Prostate CR 541	The second second second
pl2 D8587 24 9 0.38 Prostate CR 54:0	W-OWO-VANDAMA-T

Chromosome 8 - p Arm

p12	D8587	20	-5	0.25	Prostate	0 11:2121
p12	D8S87	18	4	0.22	Prostate	AJP 144:1
p12	D8987	4	4	1	Sarcoma	AJP 144:1
p12	D8S87	25	5	0.2	Uterus	CR 54:4294
Unknown	D85255	28 ***	10	0.36	Prostate	
Unknown	D8S255	10	1	0.1	Testis	CR 56:6061
11.2	ANKL	78	18	0.23	Colon	BJC 70:18
11.2	ANK1	7	4	0.57	Prostate	AJP 144:1
11.2	ANK1	1	0	0	Sarcoma	AJP 144:1
11.2122	D8S194	40	6	0.15	Colon	CR 52:5368
11.2122	D8S194	40	*5	0.17	Colon	CR 53:1172
11.2122	D8S194	4.5	5	0.11	Liver	CR 52:5368
11.2122	D89194	45	5	0.11	Liver	GCC 7:152
11.2122	D8S194	26	3	0.12	Prostate	CR 53:3869
11.2223	D8S234	58	111	0.22	Colon	CR 53:1172
11.2223	D8S234	57	14	0.25	Liver	GCC 7:152
11.22-:23	D85234	13	3	0.23	Lung	GCC 7:85
11.2223	D8S234	15	2	0.13	Prostate	GCC 13:168
23.23	D8\$140	33	6	0.18	Colon	CR 52:5368
23.23	D8S140	29	8	0.28	Colon	CR 53:1172
23.23	D89140	39	7	0.18	Liver	GCC 7:152
23.23	D8S140	39	7	0.18	Liver	CR 52:5368
23.23	D8\$140	38	4	0.11	Prostate	CR 53:3869
11.0-12	POLB	15	0	0	Colon	GCC 10:1
12-11.2	PLAT	7	2	0.29	Prostate	GCC 3:215
12-11.2	PLAT	18	0	0	Prostate	0 11:2121
11.23	D8S223	24	0	0	Colon	CR 53:1172
11.23	D8S223	37	0	0	Liver	GCC 7:152
11.23	D85223	37	0	0	Liver	GCC 7:152
Unknown	D8S:262-261	26	17	0.65	Bladder	CR 55:5213
Unknown	DBS2	5	2	0.4	Breast	CR 53:3804
Unknown	D8526	27	1	0.04	Breast	CR 53:4356
Unknown	D89349	18	10	0.56	Breast	CR 55:4995
Unknown	D8S264-D8S265-	22	4	0.18	Kidney	PNAS 92:2854
	D8S560					
Unknown	D8S264-D8S265- D8S560	6	1	0.17	Kidney	PNAS 92:2854
Unknown	D8S238	37	7	A 10		20.53.535
21	ARDRA3	19	5	0.19	Liver	CR 52:5368
Unknown	D8S339	28	************	0.26	Ovary	IJC 54:546
22-21.3	D8S360	11	10	0.36	Prostate	CR 54:6061
Unknown	D8S18	18	***************************************	0.45	Prostate	0 11:2121
SUM	20310	5603	0	0	Testis	G 5:134
200		2003	1838	0.33		

Chromosome 8 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
Unknown	D8S260	28	7	0.25	Prostate	CR 54:6061
g22	D8S167	35	4	0.11	Prostate	CR 54:6061
<u> Vaknown</u>	D85257	16	0	0	Read&Neck	CR 54:4756
Unknown	D8S257	20	8	0.4	Head&Neck	CR 54:1152
Unknown	D89257	:-14	0	0	HeadsNeck	CR 54:4756
Unknown	D8S257	6	3	0.5	Kidney	GCC 12:76
Unknown	D8S257	26	2	0.08	Melanoma	CR 56:589
Unknown	D8S257	31	17	0.55	Prostate	CR 54:6061
Onknown	D89273	30	- 6	0.2	Cervix	CR 56:1979***
Unknown	D85273	19	3	0.16	Head&Neck	CR 54:1152
Unknown	D85284	21	5	0.24	Cervix	CR 56:197
24	TG	2	0	0	Neuroblastor a	
24	TG	14	. 4	0.29	Ovary	CR 53:2393
24	TG	9	0	0	Prostate	G 11:530
24	TG		0	Ç	Prostate	GCC 3:215
24	D8S39	14	1	0.07	Breast	CR 50:7184
24	D8839	14	0	0	Cervix	CR 54:4481
24	D8S39	5	0	0	Cervix	GCC 9:119
24	D8539	9	- 0	0	Esophageal	CR 51:2113.
24	D8S39	22	0	0	Esophageal	CR 54:2996
24	D8939	. 12	1	0.08	Kidney	CR 51:820
24	D8S39	20	4	0.2	Liver	CR 51:89
24	D8S39	1	i	1	Lung	CR 52:2478
24	D8S39	3	1	0.33	Luna	CR 52:2478
24	D8939	В	1	0.12	Lung	CR 52:2478
24	D8S39	1	1	1	Lung	CR 52:2478
24	D8539	16	5	0.31	Ovary	CR 51:5118
24	D8S39	7	0	0	Prostate	GCC 3:215
24	D8539	17	2	0.12	Prostate	CR 53:3869
24	D8539	14	1	0.07	Sarcoma	CR 52:2419
24	DBS39	18	4	0.22	Testis	0 9:2245
24	D8539	8	0	0	Uterus	GCC 9:119
24	D8939	8	0	O	Uterus	GCC 9:119
Unknown	Unknown	25	0	0	Brain	CR 50:5784
22-23	Unknown	2	.0	0	Cervix	BJC 67:71
Unknown	D8S272	15	0	0	Endocrine	CR 56:599
Unknown	D8S177	42	4	0.1	Esophageal	GCC 10:177
Unknown	D8S272-D8S284	6	0	0	Kidnev	PNAS 92:2854
Unknown	D89272-D85284	21	1	0.05	Kidney	PNAS 92:2854
Unknown	D85:272-281	21	2	0.1	Leukemia	CR 55:5377
22-QTER	D8S161	19	5	0.26	Ovary	BJC 69:429
Unknown	D8S198	22	1	0.05	Uterus	CR 54:4294
Onknown	D8584	20	0	0	Uterus	CR 54:4294
SUM		661	94	0.14		

Chromosome 9 - p Arm

Dinknown	Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
OFFICAL Design St. L. O.16	Onknown	D9S143	33	17	The second secon		
222-21	Unknown	D9S129	33	18			***************************************
22-PTER	22-24	D9554	61	11	0.18	The state of the s	CONTRACTOR OF THE PROPERTY OF
Direction D99132 5	22-PTER	D9S54	10	3			and the second s
Diknown	Onknown	D99132	. 5	1		THE RESERVE OF THE PERSON NAMED IN	*3/2/47/19
Diknown	Unknown	D9S132		0			
Diknown DSS199 10	Unknown	D9S199	21	15	A ANGLE STATE STATE OF THE PARTY OF THE PART		***************************************
Onknown D95199 12 2 0.17 Ovary Oilil245 Onknown D95199 33 17 0.52 Ovary BJC 73:420 Unknown D95324 23 2 0.09 Ovary CR 55:2150 Oknown D95144 12 1 0.08 Ovary Oilil249 Oknown D95144 12 1 0.08 Ovary Oilil249 Oknown D95144 12 1 0.08 Ovary Oilil249 Oknown D95144 8 3 0.038 Ovary Oilil249 Oili	Unknown	D9S199					AND ASSESSMENT OF THE PROPERTY
Unknown D95199 33 17 0.52 Ovary BJC 73:420	Unknown	D95199	12		-	THE REAL PROPERTY AND ADDRESS OF THE PARTY AND	
Unknown D95124 23 2 D109 CV31V CR.55.2150 Unknown D95144 12 1 0.08 CV31V 0.11:1249 Unknown D95144 12 1 0.08 CV31V 0.11:1249 Unknown D95144 12 1 0.08 CV31V 0.11:1249 Unknown D95144 12 1 0.08 CV31V 0.11:1249 Unknown D95144 12 1 0.08 D340 CR.54:1397 Unknown D9514 19 4 0.21 Brain CR.54:1397 Unknown D9514 19 4 0.21 Brain CR.54:1397 Unknown D9514 19 4 0.21 Brain CR.54:1397 Unknown D9514 19 4 0.21 Brain CR.54:1397 Unknown D9514 19 4 0.21 Brain CR.54:1397 Unknown D9514 19 4 0.21 Brain CR.54:1397 Unknown D9514 19 4 0.31 Esophageal CL.97:129 Unknown D9514 2 0 0 Kidney JUCR 66:795 Unknown D9514 2 0 0 Kidney JUCR 66:795 Unknown D9514 15 8 0.53 Ovary GC.55:26 Unknown D9514 15 8 0.53 Ovary CR.55:276 Unknown D9514 15 8 0.53 Ovary GC.55:276 Unknown D9514 19 0.58 Ovary EJC.73:420 Unknown D9514 D95 D95 Ovary EJC.73:420 Unknown D9514 D95 D95 D95 Unknown D9515 D95 D95 D96 D96 Unknown D9515 D95 D95 D96 Unknown D9515 D95 D96 D96 Unknown D9515 D96 D96 D96 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9515 D96 D97 D97 Unknown D9915 D97 D97 Unknown D9915 D97 D97 D97 Unknown D9915 D97 D97 D97 Unknown D9915 D	Unknown	D9S199	***********		***************************************		***************************************
Onknown D95144 12	Unknown	D9S324			CONTROL OF CONTROL OF	eranamatan dan menangan berasalah dan menangan berasalah dan menangan berasalah dan menangan berasalah berasalah dan menangan berasalah	
Discours	Unknown	D9S144					***************************************
22	Unknown	CONTRACTOR SECTION SEC			***************************************	and the same of th	
22 IFNA 12 1 0.08 Brain CR 54:23973			***********				
22	22	A CONTRACTOR OF THE PARTY OF TH		The state of the s			70-7-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1
TINA BP 21 C.24 Breast IJC 64.378		*****					***************************************
Unknown	22	-			CONTROL TO A TOTAL CONTROL TO A STATE OF THE PARTY OF THE	A STATE OF THE PARTY OF THE PAR	
22 IFWA 2 0 0 0 Kidney GCC 12:76	Unknown	***************************************			***************************************	**************************************	
Unknown	CONCERNO A CONCERNO AND AND AND AND AND AND AND AND AND AND		THE PROPERTY OF THE PARTY OF		7 (CONT. CON	يوو وهوريونين ۾ ريانيو، هنهندي ۾ ڏهنٽن تي ۾ جي سنب	The second section is not a second section of the second section is not a second section in the second section is not a second section in the second section is not a second section in the second section in the second section is not a second section in the second section in the second section is not a second section in the second section in the second section is not a second section in the second section in the second section is not a second section in the second section in the second section is not a section in the second section in the second section is not a section in the second section in the second section is not a section in the second section in the section is not a section in the second section in the second section is not a section in the section in the section is not a section in the section is not a section in the section in the section is not a section in the section in the section is not a section in the section in the section is not a section in the section in the section is not a section in the section is not a section in the section in the section is not a section in the section in the section is not a section in the section in the section is not a section in the section in the section is not a section in the section in the section is not a section in the section in the section is not a section in the section in the section is not a section in the section in the section is not a section in the section in the section in the section is not a section in the section in the section in the section in the section is not a section in the section in the section in the section is not a section in the section
Diknown IFNA 6 5 0.83 Lung CR 55:28					***************************************		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
Unknown IFNA 15 8 0.53 Ovary GO 55:245 Unknown IFNA 28 3 0:11 Ovary CR 55:2150 Unknown IFNA 33 19 0.58 Ovary BJC 73:420 22 IFNA 58 20 0:34 Ovary AJHG 55:143 Unknown IFNA 7 0 0 Ovary O:11:1249 Unknown IFNA 3 0 0 Ovary O:11:1249 Unknown IFNA 3 0 0 Ovary O:11:1249 Unknown IFNA 3 0 0 Ovary O:11:1249 Unknown IFNA 3 0 0 Ovary O:11:1249 22 IFNA 19 5 0.26 Stomach CR 55:1933 Onknown IFNB 252 153 0.61 Bladder CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:4356 22 IFNB1 12 1 0.08 Carvix CR 54:4361 22 IFNB1 12 1 0.08 Carvix CR 54:4361 22 IFNB1 44 0 0 Leukemia AHEM 68:171 22 IFNB1 44 0 0 December AHEM 68:171 22 IFNB1 44 0 0 December AHEM 68:171 22 IFNB1 7 5 0.71 Tastis 0.9:2245 Unknown D9S156 126 30 0.24 Breast IJC 64:378 Unknown D9S156 18 13 0.72 Head6Neck CR 54:1152 Unknown D9S156 18 13 0.72 Head6Neck CR 54:1152 Unknown D9S156 13 4 0.31 Ovary 0.11:1249 Unknown D9S156 13 4 0.31 Ovary 0.11:1249 Unknown D9S157 134 0.23 Breast IJC 64:378 Unknown D9S157 134 0.23 Breast IJC 64:378 21 D9S157 135 6 0.466 Esophageal CL 97:129	The state of the s	CONTRACTOR CONTRACTOR AND ADDRESS OF THE PARTY OF THE PAR	TOO MOTHER BURGUES COMES FROM				
Unknown IFNA 28 3 0.11 Ovary CR 55:2150 Unknown IFNA 33 19 0.58 Ovary BUC 73:420 22 IFNA 58 20 0.34 Ovary AJHG 55:143 Unknown IFNA 7 0 0 Ovary 0 11:1249 Unknown IFNA 3 0 0 Ovary 0 11:1249 Unknown IFNA 3 0 0 Ovary 0 11:1249 Unknown IFNA 3 0 0 Ovary 0 11:1249 22 IFNA 19 5 0.26 Stomach CR 55:193 Onknown IFNB 252 153 0.61 Bladder CR 53:1230 Unknown IFNB 6 0 0 Breast GCC 2:191 22 IFNB1 1 0 0 Breast GCC 2:191 22 IFNB1 42 5 0.12		and the second s	************************				
Unknown	Unknown	CONTRACTOR CONTRACTOR	CONTRACTOR CONTRACTOR	7		yana maka anda ana ana ana ana ana ana ana ana a	The second secon
TENA 58 20 0.34 Ovary AJHG 55:143	and the second of the second o		*********			***************************************	***************************************
Unknown IFNA 7 0 0 Ovary 0 li:1249 Unknown IFNA 3 0 0 Ovary 0 li:1249 22 IFNA 19 5 0.26 Stomach CR 55:1933 Onknown IFNB 252 153 0.61 Bladder CR 53:1230 22 IFNB1 252 153 0.61 Bladder CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:1230 22 IFNB1 1 0 C Breast CCC 2:191 22 IFNB1 12 1 0.08 Cervix CR 54:4481 22 IFNB1 44 0 0 Prostate G 11:530 22 IFNB1 7 5 0.71	THE RESIDENCE OF STREET, AND ADDRESS OF THE PARTY OF THE	TOTAL CONTRACTOR CONTR	TO THE OWNER OF THE PARTY OF TH		THE RESERVE OF THE PARTY OF THE	andre ar varia en útica anoma mescale	
Unknown IFNA 3 0 0 Ovary 0.11-1249 22 IFNA 19 5 0.26 Stomach CR 55:1933 Unknown IFNB 252 153 0.61 Bladder CR 53:1230 22 IFNB1 252 153 0.61 Bladder CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:1230 Unknown IFNB1 1 0 0 Breast CR 54:4481 22 IFNB1 12 1 0.08 Carvix CR 54:4481 22 IFNB1 44 0 0 Leukemia AHEM 68:171 22 IFNB1 7 5 0.71 Testis 0 9:2245 Unknown D9S156 126 30		************	CONTRACTOR NAME OF STREET	***********************	***************************************	***************************************	**************************************
22 IFNA 19 5 C.26 Stomach CR 55:1933	Unknown	\$255.000 \$ \$255.00 \$255.00 \$255.00 \$255.00 \$255.00 \$255.00 \$255.00 \$255.00 \$255.00 \$255.00 \$255.00 \$255.00 \$25				areas a constantino de la constantino de la constantino de la constantino de la constantino de la constantino de	The second secon
Onknown IFNB 252 153 0.61 Bladder CR 53:1230 22 IFNB1 252 153 0.61 Bladder CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:1230 22 IFNB1 1 0 0 Breast GCC 2:191 22 IFNB1 12 1 0.08 Cervix CR 54:4481 22 IFNB1 42 5 0.12 Leukemia AHEM 68:171 22 IFNB1 4 0 0 Prostate G 11:530 22 IFNB1 7 5 0.71 Testis 0 9:2245 Unknown D9S156 126 30 0.24 Breast IJC 64:378 Unknown D9S156 18 13 0.72 Head&Neck CR 54:1152 Onknown D9S156 3 0					****************		***************************************
22 IFNB1 252 153 0.61 Bladder CR 53:1230 Unknown IFNB 6 0 0 Breast CR 53:4356 22 IFNB1 1 0 0 Breast GCC 2:191 22 IFNB1 12 1 0.08 Carvix CR 54:4481 22 IFNB1 42 5 0.12 Leukemia AHEM 68:171 22 IFNB1 44 0 0 Description AHEM 68:171 22 IFNB1 6 0 0 Prostate G 11:530 22 IFNB1 7 5 0.71 Testis O 9:2245 Unknown D9S156 126 30 0.24 Breast IJC 64:378 Unknown D9S156 18 13 0.72 Head6Neck CR 54:1152 Unknown D9S156 18 13 0.72 Head6Neck CR 54:1152 Unknown D9S156 13 4 </td <td>CONTRACTOR CONTRACTOR /td> <td>COST STORES OF MAIN PROCESS OF STREET</td> <td></td> <td>The second control of the second control of</td> <td>CONTRACTOR OF COMMENT AND ADDRESS OF THE PARTY OF THE PAR</td> <td>CONTRACTOR OF A STATE OF THE PARTY OF THE PA</td> <td>THE PROPERTY AND DESCRIPTION OF THE PROPERTY O</td>	CONTRACTOR CONTRACTOR	COST STORES OF MAIN PROCESS OF STREET		The second control of the second control of	CONTRACTOR OF COMMENT AND ADDRESS OF THE PARTY OF THE PAR	CONTRACTOR OF A STATE OF THE PARTY OF THE PA	THE PROPERTY AND DESCRIPTION OF THE PROPERTY O
Unknown IFNB 6 0 0 Breast CR 53:1230 22 IFNB1 1 0 0 Breast GCC 2:191 22 IFNB1 12 1 0.08 Cervix CR 54:4481 22 IFNB1 42 5 0.12 Leukemia AHEM 68:171 22 IFNB1 44 0 0 Leukemia AHEM 68:171 22 IFNB1 6 0 0 Prostate G 11:530 22 IFNB1 7 5 0.71 Testis 0 9:2245 Unknown D9S156 126 30 0.24 Breast IJC 64:378 Unknown D9S156 11 4 0.36 Esophageai CL 97:129 Unknown D9S156 18 13 0.72 Head4Neck CR 54:1152 Unknown D9S156 3 0 0 Ovary 0 11:1249 Unknown D9S156 13 4		******************************	*******************	200 - 100 -			······································
22 IFNB1 1 0 0 Breast CR 53;4356 22 IFNB1 12 1 0.08 Cervix CR 54;4481 22 IFNB1 42 5 0.12 Leukemia AHEM 68:171 22 IFNB1 44 0 0 Leukemia AHEM 68:171 22 IFNB1 7 5 0.71 Testis 0 9:2245 Unknown D9S156 126 30 0.24 Breast IJC 64:378 Unknown D9S156 11 4 0.36 Esophageal CL 97:129 Unknown D9S156 18 13 0.72 Head4Neck CR 54:1152 Unknown D9S156 3 0 0 Ovary 0 11:1249 Unknown D9S156 13 4 0.31 Ovary 0 11:1249 Unknown D9S157 133 30 0:23 Breast IJC 64:378 21 D9S157 13 <td< td=""><td>- 10000 Act SOCKERS CONTRACTOR SERVICES</td><td>CONTRACTOR OF CONTRACTOR COMPANY</td><td>ACT TO SERVICE OF THE PARTY OF</td><td>COLD COLD AND AND CONTRACT OF COLD AND AND AND AND COM-</td><td>STATE TO COMPANY TO STATE OF THE PARTY OF TH</td><td></td><td></td></td<>	- 10000 Act SOCKERS CONTRACTOR SERVICES	CONTRACTOR OF CONTRACTOR COMPANY	ACT TO SERVICE OF THE PARTY OF	COLD COLD AND AND CONTRACT OF COLD AND AND AND AND COM-	STATE TO COMPANY TO STATE OF THE PARTY OF TH		
Z2 IFNB1 12 1 0.08 Carvix CR 54:44B1 22 IFNB1 42 5 0.12 Leukemia AHEM 68:171 22 IFNB1 44 0 0 Leukemia AHEM 68:171 22 IFNB1 6 0 0 Prostate G 11:530 22 IFNB1 7 5 0.71 Testis 0 9:2245 Unknown D9S156 126 30 0.24 Breast IJC 64:378 Unknown D9S156 11 4 0.36 Esophageai CL 97:129 Unknown D9S156 18 13 0.72 Head4Neck CR 54:1152 Unknown D9S156 3 0 0 Ovary 0 11:1249 Unknown D9S156 13 4 0.31 Ovary 0 11:1249 21 D9S157 133 30 0.23 Breast IJC 64:376 21 D9S157 13 6 <td></td> <td></td> <td>ALIER AND METHOD SECTION SECTI</td> <td>A STATE OF THE PARTY OF THE PAR</td> <td>Accessor (1997)</td> <td>AND THE RESIDENCE OF THE PROPERTY OF THE PROPE</td> <td>***************************************</td>			ALIER AND METHOD SECTION SECTI	A STATE OF THE PARTY OF THE PAR	Accessor (1997)	AND THE RESIDENCE OF THE PROPERTY OF THE PROPE	***************************************
22 IFNB1 42 5 0.12 Leukemia AHEM 68:171 22 IFNB1 44 0 0 Leukemie AHEM 68:171 22 IFNB1 6 0 0 Prostate C 11:530 22 IFNB1 7 5 0:71 Testis O 9:2245 Unknown D9S156 126 30 0.24 Breast IJC 64:378 Unknown D9S156 11 4 0.36 Esophageal CL 97:129 Unknown D9S156 18 13 0.72 Head4Neck CR 54:1152 Unknown D9S156 3 0 0 Ovary O 11:1249 Unknown D9S156 13 4 0.31 Ovary O 11:1249 Unknown D9S156 13 4 0.31 Ovary O 11:1249 Unknown D9S157 133 30 0:23 Breast IJC 64:378 21 D9S157 13	. Committee and the committee of the com	CONTRACTOR OF THE PARTY OF THE		AND STORE OF BOOKING AN ALL COMPANIES AND ALL CO	A TO STATE OF THE PARTY OF THE	CONTRACTOR OF THE PARTY OF THE	Maria Mariana
22 IFNB1 44 0 0 Leukemia AHEM 68:171 22 IFNB1 6 0 0 Prostate G 11:530 22 IFNB1 7 5 0.71 Testis 0 9:2245 Unknown D9S156 126 30 0.24 Breast IJC 64:378 Unknown D9S156 11 4 0.36 Esophageal CL 97:129 Unknown D9S156 18 13 0.72 Head4Neck CR 54:1152 Unknown D9S156 3 0 0 Ovary 0 11:1249 Unknown D9S156 13 4 0.31 Ovary 0 11:1249 Unknown D9S157 133 30 0:23 Breast IJC 64:376 21 D9S157 30 5 0.17 Cervix CR 56:197 21 D9S157 13 6 0:46 Escphageal CL 97:129		Access to the contract of the			The second secon		
22 IFNB1 6 0 0 Prostate G 11:530 22 IFNB1 7 5 0.71 Testis 0 9:2245 Unknown D9S156 126 30 0.24 Breast IJC 64:378 Unknown D9S156 11 4 0.36 Esophageal CL 97:129 Unknown D9S156 18 13 0.72 Head6Neck CR 54:1152 Unknown D9S156 3 0 0 Ovary 0 11:1249 Unknown D9S156 13 4 0.31 Ovary 0 11:1249 Unknown D9S156 13 4 0.31 Ovary 0 11:1249 Unknown D9S157 133 30 0:23 Breast IJC 64:378 21 D9S157 30 5 0.17 Cervix CR 56:197 21 D9S157 13 6 0:46 Escphageal CL 97:129		to Publish the processor and processor and			THE STREET STREET, SALES OF THE STREET, SALES	CONTRACTOR OF THE PARTY OF THE	NO CONTROL OF THE PARTY OF THE
22 FFNB1 7 5 0.71 Testis O 9:2245 Unknown D9S156 126 30 0.24 Breast IJC 64:378 Unknown D9S156 11 4 0.36 Esophageal CL.97:129 Unknown D9S156 18 13 0.72 Head4Neck CR 54:1152 Unknown D9S156 3 0 0 Ovary 0.11:1249 Unknown D9S156 13 4 0.31 Ovary 0.11:1249 Unknown D9S157 133 30 0:23 Breast IJC 64:378 21 D9S157 30 5 0.17 Cervix CR 56:197 21 D9S157 13 6 0:46 Escphageal CL 97:129		· · · · · · · · · · · · · · · · · · ·				Market	\$45 - 444 - 444 - 444 - 444 - 444 - 444 -
Unknown D9S156 126 30 0.24 Breast IJC 64:378 Unknown D9S156 11 4 0.36 Esophageal CL 97:129 Unknown D9S156 18 13 0.72 Head6Neck CR 54:1152 Onknown D9S156 3 0 0 Ovary 0.11:1249 Unknown D9S156 13 4 0.31 Ovary 0.11:1249 21 D9S157 131 30 0.23 Breast IJC 64:378 21 D9S157 30 5 0.17 Cervix CR 56:197 21 D9S157 13 6 0.46 Escphageal CL 97:129	··· COTTOTO O DISTRICTION CONTRACTOR	STEERSEN TO SOME AND A PROPERTY			•	THE RESERVE OF THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN	
Unknown D9S156 11 4 0.36 Esophageal CL 97:129 Unknown D9S156 18 13 0.72 Head6Neck CR 54:1152 Unknown D9S156 3 0 0 Ovary 0 11:1249 Unknown D9S156 13 4 0.31 Ovary 0 11:1249 21 D9S157 133 30 0:23 Breast IJC 64:378 21 D9S157 30 5 0.17 Cervix CR 56:197 21 D9S157 13 6 0:46 Escphageal CL 97:129 21 D9S157 13 6 0:46 Escphageal CL 97:129		***************************************			**************************************	***********************	***************************************
Unknown D9S156 18 13 0.72 Head4Necx CR 54:1152 Unknown D9S156 3 0 C Ovary 0:1:1249 Unknown D9S156 13 4 0.31 Ovary 0:1:1249 21 D9S157 133 30 0:23 Breast IJC:64/378 21 D9S157 30 5 0.17 Cervix CR 56:197 21 D9S157 13 6 0.46 Escphageal CL 97:129	- color accident a segment of the segment	PERSONAL PROPERTY AND ARREST			THE PERSON NAMED OF THE PERSON OF THE PERSON NAMED OF THE PERSON N	THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NAMED IN COLUMN TWO IS NAMED IN COLUMN TWO IS NAMED IN COLUMN TWO IS NAMED IN COLUMN TWO IS NAMED IN COLUMN TWO IS NAMED IN COLUMN TWO IS NAMED IN COL	****
Onknown D9S156 3 0 0 Ovary 0 1:1249 Unknown D9S156 13 4 0.31 Ovary 0 1:1249 21 D9S157 133 30 0:23 Breast IJC:64/378 21 D9S157 30 5 0.17 Cervix CR 56:197 21 D9S157 13 6 0:46 Escphagea) CL 97:129		and the second of the second o	Andrew Commence of the Commenc			************	
Unknown D9S156 13 4 0.31 Ovary 0 11:1249 21 D9S157 133 30 0:23 Breast IJC:64:378 21 D9S157 30 5 0.17 Cervix CR 56:197 21 D9S157 13 5 0.46 Escophageal CL 97:129	CONTRACTOR AND ADDRESS OF THE PROPERTY OF THE PARTY OF TH	CONTRACTOR AND ADDRESS OF A STREET		and a first of the state of the	CONTRACTOR CONTRACTOR OF CONTRACTOR	CONTRACTOR CONTRACTOR AND AND AND AND AND AND AND AND AND AND	
21 D9S157 133 30 0:23 Breast IJC 64/378 21 D9S157 30 5 0.17 Cervix CR 56:197 21 D9S157 13 6 0.46 Escphageal CL 97:129	* ** * ** * * * * * * * * * * * * * *	Company of the Compan		***************************************		· · · · · · · · · · · · · · · · · · ·	
21 D9S157 30 5 0.17 Cervix CR 56:197 21 D9S157 13 6 0.46 Eschlageal CL 97:129	Commences a commence and a comme	CAPP 9000 9,000 block occurrence comme			7799.CCCC799040900000000000000000000000000000	anno en constituis de la constant	THE PROPERTY OF THE PARTY OF TH
21 D99157 13 6 0.46 Escphageal CL 97:129		and the second s	******************************	CONTRACTOR OF THE PROPERTY OF	***************************************	CONTRACTOR OF STREET	******************************
21 000157		TO SEE THE PROPERTY OF THE PRO		2	THE RESERVE WAS A STREET OF THE PARTY OF THE	CONTRACTOR OF THE PARTY OF THE	
25 0.36 Esophageal IJC 69:1		AND THE PROPERTY OF THE PARTY O	************	CONTRACTOR OF THE PROPERTY OF			
	~ *	U3313/	65	25	0.38	Esophageal	IJC 69:1

Chromosome 9 - p Arm

21	D9S157	5	1	0.2	Kidney	
Unknown	D9S168	120	17	0.14	Breast	GCC 12:76
Unknown	D96168	33	15			IJC 64:378
21	CDKN2	109	20	0.18	Overy	BJC 73:420
.21	p15-p16	50	28	0.15	Bladder	JNCI 87:1524
21	CDKN2	55	1	0.02	Esophageal	
21	CDKN2	34	7	0.02	Kidney	JJCR 86:795
21	CDKN2	50	24	0.48	Lung	GCC 14:164
21	p15-p16	56	3	0.05	Ovary	IJC 63:222
21	MTS2	100	18	0.18	Sarcoma	CGC_86:136
21	D95162	90	10	0.18	Bladder	JNCI 87:1524
21	D9S162	9	3	0.33	Breast	IJC 64:378
21	D9S162	33.	4	0.12	Esophageal	CL 97:129
21	D9S162	41	13	0.32	<u>Head&Neck</u>	The state of the s
21	D95162	4	. 0	0.32	Head&Neck	CR 54:4756
21	D9S162	33	17	0.52	Kidney	GCC 12:76
21	D9S162	12	1	0.52	Ovary	BJC 73:420
21	D9S162	15	3	0.2	Ovary	0 11:1249
21	D95171	139	28	0.2	Ovary	0 11:1249
21	D9S171	60	19		Breast	IJC 64:378
21	D9S171	11	13	0.32 0.36	Esophageal	IJC 69:1
21	D9S171	3	0	U.36 0	Esophageal	CL 97:129
21	D95171	12	3	0.25	Kidney	GCC 12:76
Unknown	D9S:162-171	6	3	0.25	Kidney	JJCR 86:795
21	D9S171	24	4	0.17	Kidney	GCC 12:76
21	D9S171	8	5	0.62	Lung	GCC 14:164
Unknown	D98:162-171	35	16	CONCERNO CONTRACTOR OF CONTRAC	Lung	CR 54:2307
21	D9S171	9	3	0.46 0.33	Melanoma	CR 56:589
21	D9S171	33	16	0.33	Ovary	0 11:1249
21	D9S171	15	1	0.07	Ovary	BJC 73:420
Unknown	D95126	252	152	0.07	Ovary	0 11:1249
Unknown	D9S126	252	152	0.6	Bladder	CR 53:1230
Unknown	D9S126	80	152	0.19	Bladder	CR 53:1230
Unknown	D9S126	16	3	0.19	Breast	IJC 64:378
Dukuchu	IFN2a- D9S126	5	5	1	Endocrine	CR 56:599
Unknown	D9S126	9	0	0	Lung	CR 55:513
Unknown	D9S126	īi .	i	0.09	Ovary	0 11:1249
Unknown	D9S126	51	17	0.33	Ovary	0 11:1249
Unknown	D95126	30	3	MANAGE CO. OF STREET, ST. ST. ST. ST. ST. ST. ST. ST. ST. ST.	Ovary	AJHG 55:143
Unknown	D9S126	33	17	0,1	Ovary	CR 55:2150
Unknown	D9S736	33	18	0.52	Ovary	BJC 73:420
Unknown	D9S3	252	154	0.55	Ovary	BJC 73:420
21	D9S3	16	33	0.61	Bladder	CR 53:1230
21	D9S3	4	1	0.19	Bladder	CR 54:2848
21	D9S169	22	4	0.25	Breast	CR 53:3804
21	D9S169	8	4	0.18	Cervix	CR 56:197
		Ü	0	0.75	Lung	CR 54:2307

Chromosome 9 - p Arm

21	S161	15	5	0.33	Esophageal	CL 97:129
21	S161	5	1	0.3		GCC 12:76
21	9161	10	2	0.2	Kidney	
21	S161	14	۵	0	Ovary	0 11:1249
Unknown	D9S104	117	20	0.17	Ovary	0 11:1249
Unknown	D9S104	63	27	0.43	Breast	IJC 64:378
Unknown	D95104	33	15	0.45	Esophageal	IJC 69:1
Unknown	D9S104	19	4		Ovary	BJC 73:420
21-ater	D9852	12	5	0.21	Uterus	CR 54:4294
Unknown	D9S165	4	0	0.42	Ovary	GO 55:245
Unknown	D98165	8		0	Ovary	0 11:1249
Unknown	D9S200		0	0	Ovary	0 11:1249
Unknown	D95200	11	2	0.18	Esophageal	CL 97:129
Unknown		25	13	0.52	Head&Neck	CR 54:1152
Unknown	D95200 D95200	33	13	0.39	Ovary	BJC 73:420
Unknown		13.	1	0.08	Ovary:	0.11:1249
12	D9S200	13	4	0.31	Ovary	0 11:1249
***************************************	D9855	14		0.07	Brain	CR 54:1397
12	D9S55	18	2	0.11	Brain	CR 54:1397
12	D9955	18	. 2	0.11	Brain	CR 54:1397
Unknown	D9S47	252	152	0.6	Bladder	CR 53:1230
Unknown -	IFNa- D9S:1751-	31	19	0.61	Bladder	CR 55:5213
	736-1747-1748- 1752-171					
Unknown	Unknown	12	0			
Unknown	D9S18	30	17	0 0.57	Brain	CR 50:5784
Unknown	MTS1	5	5	U.5/	Esophageal	GCC 10:177
Unknown	D9S168-D9S166		2	1	Esophageal	0 9:3737
Unknown	D9S168-D9S166	19	<u>د</u> ع	0.4	Kidney	PNAS 92:2854
Unknown	D9S:168+171	50	20	0.16	Kidney	PNAS 92:2854
Unknown	Unknown	33	***************************************	0.4	Leukemia	CR 55:5377
Unknown	D9S171-D9S126-	29	17	0.52	Lung	CR 54:2322
	D9S169	23	17	0.59	Lung	JCRCO 121:291
Unknown	D9S171-D9S126-	6	0	0	I una	JCRCO 121:291
	D9S169	J	U	U	Lung	JURCO 121:291
Unknown	D9S171-D9S126-	47	10	0.21	Lung	JCRCO 121:291
	D9S169					00.00 121.231
Unknown	OVC	15	5	0.33	Ovary	CR 53:2393
SUM		4921	1868	0.38		

Chromosome 9 - q Arm

Onknown D9515 10 10 10 10 10 10 10	Band	Marker	Total	Cases w/LOH	LOH Frag.	Tumor Type	Reference
District District	Onknown	D9915	70	37	the Residence of the second second second second	CONTRACTOR OF STREET,	Constitution of the Consti
13-21.1 D9515 6	Unknown	D9S15	11	1	0.09		
13-21.1 D9515 14 1 0.07 Esophageal CR 54:2996	13-21.1	D9515	6	3	0.5	THE CONTRACT AND DESCRIPTION OF THE PARTY OF	
Distribution Dist	13-21.1	D9S15	14	1	0.07		
Unknown	Unknown	D9915	22	9. "9	0.41	Carlo de la constanti de la co	
13-21.1 D9515 6	Unknown	D9S15	12	2		***************************************	The state of the s
Unknown	13-21.1	D9S15	- 6	1			CONTRACTOR OF CO
13-21-1	Unknown	D9S15	8	1			
Unknown D9S15	13-21.1	D9915	14		THE TAX AND ADDRESS OF THE PARTY OF THE PART	THE PERSON NAMED IN COLUMN TWO IS NOT THE OWNER, THE OW	CONTRACTOR OF THE PROPERTY OF
Unknown D9515 16 2 0:12 Ovary CR:55:2150 Unknown D9515 33 15 0.45 Ovary BJC 73:420 Dnknown D9915 10 3 0.3 Sarcoms GR:52:2419 13-21.1 D9515 10 2 0.2 Uterus GCC 9:119 Unknown D9518 Z52 151 0.6 Bladder CR:53:1730 Unknown D9518 7 0 0 Cervix GCC 5:119 Unknown D9518 7 0 0 Cervix GCC 5:119 Unknown D9518 13 4 0.31 Ovary JJC 54:546 Unknown D9518 13 4 0.31 Ovary JJC 54:546 Unknown D9518 16 1 0.06 Urerus GCC 9:119 Unknown D9527 8 2 0.25 Testis 0 9:2245 Unknown D9510 33 16 0.48 Ovary BJC 73:420 Unknown D9510 33 16 0.48 Ovary BJC 73:420 Unknown D9516 8 2 0.25 Dvary 0.117:249 Unknown D9516 8 2 0.25 Dvary 0.117:249 Unknown D9516 8 2 0.25 Dvary 0.117:249 Unknown D9516 8 2 0.25 Dvary 0.117:249 Unknown D9516 3 0 0 Ovary 0.117:249 Unknown ASSP3 8 0 0 Ovary DJC 69:429 Unknown ASSP3 8 0 0 Cervix CCC 48:72 Unknown ASSP3 8 0 0 Cervix CCC 48:72 Unknown ASSP3 8 0 0 Cervix CR 48:2988 Unknown ASSP3 8 0 0 Cervix CR 48:2988 Unknown ASSP3 8 0 0 Cervix CR 48:3598 Eter-ql1 D951 7 0.37 Ovary BJC 69:429 Unknown BJS 3 10 33 0.53 Bladder O.11:1671 Deter-ql1 D951 7 0 0 Cervix CR 49:3598 Deter-ql1 D951 7 0 0 Cervix CR 49:3598 Deter-ql1 D951 7 0 0 Cervix CR 49:3598 Deter-ql1 D951 7 0 0 Cervix CR 54:2761 Deter-ql1 D951 7 0 36 D.54 Bladder O.11:1671 Duknown D95201 70 36 D.55 Bladder O.11:1671 Duknown D95201 70 36 D.55 Bladder O.11:1671 Duknown D95201 70 36 D.55 Bladder O.11:1671 Duknown D95201 70 36 D.55 Bladder O.11:1671 Duknown D95201 70 36 D.55 Bladder O.11:1671 Duknown D95201 70 36 D.55 Bladder O.11:1671 Duknown D95201 70 36	Unknown	D9S15	4	······································			Martine
Unknown D9515 10 3 0.15 Sarcoma OR 52;2419 13-21.1 D9515 10 3 0.3 Sarcoma OR 52;2419 13-21.1 D9515 10 2 0.2 Uterus GCC 9:119 Unknown D9518 252 151 0.6 Rladder CR 53;1230 Unknown D9518 7 0 0 Cervix GCC 9:119 Unknown D9518 28 10 0.35 Exophagea CR 54;295 CR	Unknown	D9S15	16		***	THE REAL PROPERTY AND ADDRESS OF THE PARTY O	THE PARTY OF THE P
Dicknown Dicknown	Unknown	D9 S 15	33				
13-21.1	Onknown	D9915		MAKEN		CONTRACTOR OF THE PROPERTY OF THE PARTY OF T	
Unknown D9S18 7	13-21.1	D9S15			Committee also and committee a	***************************************	
Unknown D9518	Unknown	D9S18	252		CONTRACTOR OF THE PROPERTY OF	*********	*****
Unknown D9518 13	Unknown	D9S18					
Unknown D9518 13	Unknown	D9818	28	_			
Unknown D9S18		D9S18	13	4	************************		
Unknown D9S17	Unknown	D9S18	16	***************************************		andres and the second 	
Diknown Disio Di						*****	and the second s
Unknown D9S103 33 16 0.48 Ovary BJC 73:420	Unknown	PARTICIPATION OF THE PROPERTY OF			CONTRACTOR OF THE PARTY OF THE	THE RESERVE THE PARTY OF THE PA	account and account comments and account of the second sec
Unknown D98166 B 2 0.25 Ovary 0.11/1249 Unknown D95166 3 0 0 Ovary 0.11/1249 Unknown ASSP3 252 155 0.62 Bladder CR 53:1230 Unknown ASSP3 8 0 0 Liver CCG 48:72 11-22.0 ASSP3 19 7 0.37 Ovary BJC 69:429 11-22.0 ASSP3 8 0 0 Stomach CR 48:2988 Unknown S153 70 37 0.53 Bladder Q 11:1671 pter-ql1 D951 2 0 0 Cervix CR 49:3598 pter-ql1 D951 7 0 0 Cervix CR 49:3598 pter-ql1 D951 7 0 0 Liver JJCR 81:108 pter-ql1 D951 1 0 0 Nauroblastom CR 49:1095 pter-ql1 D951 1 0 <	Unknown			***************************************		The second secon	
Unknown	Unknown	CONTRACTOR STATE OF THE PROPERTY OF THE PROPER			THE RESERVE OF THE PARTY OF THE	THE STATE OF THE PROPERTY OF THE PARTY OF TH	
Unknown ASSP3 252 155 0.62 Bladder CR 53:1230 Unknown ASSP3 8 0 0 Liver CCG 48:72 11-22.0 ASSP3 19 7 0.37 Ovary BOC 69:429 11-22.0 ASSP3 8 0 0 Stomach CR 48:2988 Onknown \$153 70 37 0.53 Bladder 0:11:1671 pter-ql1 D9S1 2 0 0 Cervix CR 49:3598 pter-ql1 D9S1 7 0 0 Cervix CR 49:3598 pter-ql1 D9S1 7 0 0 Liver JJCR 81:108 pter-ql1 D9S1 7 0 0 Nouroblastom CR 49:1095 a. Dter-ql1 D9S1 5 0 0 Nouroblastom CR 49:1095 bter-ql1 D9S1 1 0 0 Pancreas CR 54:2761 pter-ql1 D9S1 1 0	COLOR FOR CONTRACTOR AND AND AND AND AND AND AND AND AND AND	**************************************			***************************************		
Unknown ASSP3	Unknown	Cocces de la companya del companya de la companya del companya de la companya de			***************************************	THE PERSON NAMED IN COLUMN TWO IS NOT THE OWNER, THE PERSON NAMED IN COLUMN TWO IS NOT THE OWNER, THE PERSON NAMED IN COLUMN TWO IS NOT THE OWNER, THE PERSON NAMED IN COLUMN TWO IS NOT THE OWNER, THE PERSON NAMED IN COLUMN TWO IS NOT THE OWNER, THE PERSON NAMED IN COLUMN TWO IS NOT THE OWNER, THE PERSON NAMED IN COLUMN TWO IS NOT THE OWNER, THE OWNER	
11-22.0 ASSR3 19 7 0.37 Ovary BUC 69:429 11-22.0 ASSR3 8 0 0 Stomach CR 48:2988 Unknown 5153 10 37 0.53 Bladder 0.11:1671 pter-q11 D9S1 2 0 0 Cervix CR 49:3598 pter-q11 D9S1 13 1 0.08 Colon IJC 53:382 pter-q11 D9S1 7 0 0 Liver JJCR 81:108 pter-q11 D9S1 5 0 0 Nauroblastom CR 49:1095 3 pter-q11 D9S1 1 0 0 Pancreas CR 54:2761 pter-q11 D9S1 1 0 0 Pancreas CR 54:2761 pter-q11 D9S1 14 1 0:07 Stomach CR 52:3099 pter-q11 D9S1 6 0 0 Uterus CR 51:5632 Unknown D9S167 70	Unknown		***************************************	***********************	*****		
11-22.0 ASSP3	11-22.0	COVER OF COMMON PROPERTY AND THE PROPERT			Andrewson and the factor of the same of th		
Onknown \$153 70 37 0.53 Bladder 0.11:1671 pter-qll D9S1 2 0 0 Cervix CR 49:3598 pter-qll D9S1 13 1 0.08 Colon IJC:53:362 pter-qll D9S1 7 0 0 Liver JJCR 81:108 pter-qll D9S1 5 0 0 Neuroblastom CR 49:1095 pter-qll D9S1 1 0 0 Pancreas CR 54:2761 pter-qll D9S1 14 1 0.07 Stomach CR 54:2761 pter-qll D9S1 14 1 0.07 Stomach CR 52:3099 pter-qll D9S1 6 0 0 Uterus CR 51:5632 Unknown D9S167 70 38 0.54 Bladder 0.11:1671 Unknown D9S201 26 7 0.27 Ovary GR 55:2150 Unknown D9S283 33			*****	*********************	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	***************************************	
Description Description	Unknown	S153	7.0	CO. CO. CO. CO. CO. CO. CO. CO. CO. CO.		THE PARTY OF THE P	
Description Description	pter-all	*****************************	***************************************	~~~~		ACCOUNT ACCOUNT ACCOUNT ACCOUNT ACCOUNT	· · · · · · · · · · · · · · · · · · ·
Description Description	pter-q11	D991		***************************************	************	CONTRACTOR OF SCHOOLSESS CONTRACTOR OF THE SC	ante contrato de la comunicación de contrato de la contrato de la contrato de la contrato de la contrato de la
Description Description					******************************	CONTRACTOR CONTRACTOR	**************************************
Dief-q1 D9S1 1 0 0 0 Pancreas CR 54:2761	pter=qll	D951	5		*****	THE THE THE PARTY AND ADDRESS OF THE PARTY O	to a department of the property of the propert
Description Description		***			ŭ	And the second second second second second second	M CA 33.1033
prer-q11 D9S1 14 1 0.07 Stomach CR 52:3099 pter-q11 D9S1 6 0 0 Uterus CR 51:5632 Unknown D9S167 70 38 0.54 Bladder 0 11:1671 Unknown D9S201 70 36 0.51 Bladder 0 11:1671 Unknown D9S201 26 7 0.27 Ovary CR 55:2150 Unknown D9S201 33 13 0.39 Ovary BJC 73:420 Unknown D9S283 70 37 0:53 Bladder 0 11:1671 Unknown D9S283 33 13 0.39 Ovary BJC 73:420 Unknown D9S12 70 36 0:51 Bledder 0 11:1671 Unknown D9S12 9 0 0 Colon CCG 48:167	pter-qll	D9S1	1	0	0		CR 54:2761
Design	pter-q11	D9S1	14	1	0.07	Stomach	AND THE PROPERTY OF THE PROPER
Unknown D9S167 70 38 0.54 Bladder 0 11:1671 Unknown D9S201 70 36 0.51 Bladder 0 11:1671 Unknown D9S201 26 7 0.27 Ovary GR 55:2150 Unknown D9S201 33 13 0.39 Ovary BJC 73:420 Unknown D9S283 70 37 0:53 Bladder 0 11:1671 Unknown D9S283 33 13 0.39 Ovary BJC 73:420 Unknown D9S12 70 36 0.51 Bladder 0 11:1671 Unknown D9S12 9 0 0 Colon CCG 48:167	pter-qll	D9S1	6	0			Anne 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1
Unknown D95201 70 36 0.51 Bladder 0 11:1671 Unknown D95201 26 7 0.27 Ovary CR 55:2150 Unknown D95201 33 13 0.39 Ovary BJC 73:420 Unknown D95283 70 37 0:53 Bladder 0 11:1671 Unknown D95283 33 13 0.39 Ovary BJC 73:420 Unknown D9512 70 36 0:51 Bladder 0 11:1671 Unknown D9512 9 0 0 Colon CCG 48:167	Unknown	D9S167	70	38	0.54	***************************************	
Onknown D9S201 26 7 0.27 Ovary CR 55:2150 Unknown D9S201 33 13 0.39 Ovary BJC 73:420 Unknown D9S283 70 37 0:53 Bladder 0 11:1671 Unknown D9S283 33 13 0.39 Ovary BJC 73:420 Unknown D9S12 70 36 0.51 Bladder 0 11:1671 Unknown D9S12 9 0 0 Colon CCG 48:167	Unknown	D9S201	70	******************************		***************************************	•••••
Unknown D95201 33 13 0.39 Ovary BJC 73:420 Unknown D95283 70 37 0.53 Bladder 0 11:1671 Unknown D95283 33 13 0.39 Ovary BJC 73:420 Onknown D9512 70 36 0.51 Bladder 0 11:1671 Unknown D9512 9 0 0 Colon CCG 48:167	Unknown	D9\$201	26	7	ALAK SECAND PROPERTY OF THE PROPERTY AND ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY ADDRESS OF TH		Annual des recordes a financial des descriptions de la company de la com
Unknown D9S283 70 37 0:53 Bladder 0:1:1671 Unknown D9S283 33 13 0.39 Ovary BJC 73:420 Onknown D9S12 70 36 0.51 Bladder 0:11:1671 Unknown D9S12 9 0 0 Colon CCG 48:167	Unknown	D9S201			************		*******************************
Unknown D9S283 33 13 0.39 Ovary BJC 73:420 Unknown D9S12 70 36 0.51 Bladder 0 11:1671 Unknown D9S12 9 0 0 Colon CCG 48:167	Unknown	D9S283	70	37		The second secon	
Onknown D9S12 70 36 0.51 Bladder 0.11:1671 Unknown D9S12 9 0 0 Colon CCG 48:167	Unknown	D9S283			***********************		M
Unknown D9S12 9 0 0 Colon CCG 48:167	Onknown	D9S12	70	THE PROPERTY OF THE PROPERTY O			AND AND AND AND AND AND AND AND AND AND
	Unknown	D9S12	9	***********		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
	Unknown	D9S12	33	12	0.36	OVELY	BJC 73:420

Chromosome 9 - q Arm

Unknown	D9S12	13	6	0.46	Ovary	CR 55:2150
Unknown	D95119	70	-			0 11:1671
Unknown	D9S197	6	3	0.5	Kidnev	GCC 12:76
Unknown	D9S197	26	5	0.19	Melanoma	CR 56:589
Unknown	D9S22	252	154	0.61	Bladder	CR 53:1230
Doknown	D95176	70	38	0.54	Bladder	0.11:1621
Unknown	D9S176	6	1	0.17	Kidney	GCC 12:76
Մո known	D9529	4		0.25	HeadaNeck	CL 79:67
Unknown	D9S29	19	11	0.58	Ovary	CR 55:2150
Dnknown	D95109	70	37	0.53	Bladder	0 11:1671
Unknown	D9S109	5	1	0.2	Kidney	GCC 12:76
Unknown	095109	29	6	0.21	Ovazy	CR 55:2150
Unknown	D9S127	70	36	0.51	Bladder	0 11:1671
Onknown	D9S127	24	7	0.29	Overy	CR 55:2150
Unknown	D9S127	33	18	0.55	Ovary	BJC 73:420
Unknown	D9553	70	38	0.54	Bladder	0 11:167175
Unknown	D9S53	19	3	0.16	Head&Neck	CR 54:1152
Daknown	D9S53	35	12	0.34	Ovary	CR 55:2150
Unknown	D9S53	33	19	0.58	Ovary	BJC 73:420
Unknown	D9\$53	24	1	0.04	Uterus	CR 54:4294
Unknown	D9S58	70	37	0.53	Bladder	0 11:1671
Unknown	09858	27	7	0.26	DVBXY	CR 55:2150
Unknown	D9S105	70	37	0.53	Bladder	0 11:1671
Unknown	HXB	70	39	0.56	Bladder	0 11:1671
Unknown	HXB	33	17	0.52	Ovary	BJC 73:420
Unknown	нхв	24	10	0.42	Ovary	CR 55:2150
Unknown	HXB	19	1	0.05	Uterus	CR 54:4294
Unknown	D9S155	33	15	0.45	Ovary.	BJC 73:420
Unknown	D9S16	12	6	0.5	Ovary	CR 55:2150
Unknown	09859	70	37	0.53	Bladder	0 11:1671
Unknown	D9S59	33	18	0.55	Ovary	BJC 73:420
Unknown	D9\$59	30	10	0.33	Ovary	CR 55:2150
Unknown	D9S154	70	38	0.54	Bladder	0 11:1671
Bnknown	D95154	34	5	0.15	Cervix	CR 56:197
Unknown	D9S302	36	4	0.11	Brain	CR 55:4696
Unknown	D9S302	36		0.11	Brain	CR_55:4696
Unknown	D9 S 258	70	35	0.5	Bladder	0 11:1671
33	GSN .	70	39	0.56	Bladder	0 11:1671
33	GSN	17	3	0.18	Head&Neck	CR 54:1152
33	GSN	5	0	0	Kldney	GCC 12:76
33	GSN	18	8	0.44	Ovary	BJC 69:429
Onknown	GSN	33	16	0.48	Overy	BJC 731420
33	GSN	15	7	0.47	Ovary	CR 55:2150 CR 53:1230
Unknown	D9549	252	154	0.61	Bladder	THE TANK THE PERSON NAMED IN COLUMN TO PERSO
31-34	D9S28	39	5	0.13	Bladder	CR 54:2848
31-34	D9S28	1	1	<u> </u>	HeadsNeck	CL 79:67

Chromosome 9 - q Arm

Unknown	D9S60	70	36	0.51	Bladder	0 11:1671
Unknown	D9S61	70	38	0.54	Bladder	0 11:1671
34-QTER	D9564	17	8	0.47	Ovary	BJC 69:429
Unknown	D9564	18	10	0.56	Qvary	CR 55:2150
34.1	ABL	65	13	0.2	Bladder	CR 54:2848
34.1	ABL	70	37	0.53	Bladder	0 11:1671
34.1	ABL	33	15	0.45	Ovary	BJC 73:420
34.1	ABL	25	10	Q.4	Ovary	CR 55:2150
34-gter	ASS	20	5	0.25	Bladder	CR 54:2848
34-qter	ASS	17	0	0	Brain	CR 54:1397
34-ater	ASS	12	0	0	Brain	CR 54:1397
34-qter	ASS	14	2	0.14	Lung	PN 84:9252
34-ater	ASS	34	13	0.38	Ovary	CR 55:2150
Unknown	D95164	6	1	0.17	Kidney	PNAS 92:2854
Unknown	D9S164	20	3	0.15	Kidney	PNAS 92:2854
Unknown	D9510	252	154	0,61	Blädder	CR:53:1230
34.3	D9S10	41	13	0.32	Bladder	CR 54:2848
34.3	D9S10	15	8	0.53	Ovary	CR 55:2150
Unknown	D9S66	70	38	0.54	Bladder	0 11:1671
Unknown	D9514	252	151	0.6	Bladder	CR 53:1230
Unknown	D9S67	70	36	0.51	Bladder	0 11:1671
Unknown	D9S13	252	151	0.6	Bladder	CR 53:1230
34	D9S17	35	6	0.17	Breast	CR 50:7184
34	D9517	21	16	0.76	Esophageal	GCC 10:177
34	D9S17	31	8	0.26	Lung	CR 52:2478
34	D9S17	20	2	0.1	Overy	CR 51:5118
Unknown	D9S7	252	155	0.62	Bladder	CR 53:1230
34	0987	65	13	0.2	Bladder	CR 54:2848
34	D957	7	0	0	Brain	CR 49:6572
34	D957	21	2	0.1	Breast	GCC 2:191
Unknown	D957	44	6	0.14	Breast	CR 53:4356
34	D9\$7	5	1	0.2	Breast	CR 53:3804
34	D9S7	3	2	0.67	Cervix	GCC 9:119
34	D957	33	5	0.15	Cervix	CR 54:4481
34	D9S7	20	1	0.05	Endocrine	GCC 13:9
Unknown	0987	9	0	Ð	Esophageal	CR 51:2113
34	D9S7	24	7	0.29	Esophageal	CR 54:2996
34	D957	10	1	0.1	Kidney	CR 51:820
34	D9S7	9	0	0	Liver	CR 51:89
34	0987	6	1	0.17	Liver	BJC 64:1083.
34	D9S7	11	1	0.09	Liver	BJC 67:1007
Unknown	D957	32	6	0.19	Ovary	IJC 54:546
34	D9S7	6	1	0.17	Ovary	CR 55:2150
34	D957	2	0	0	Pancreas	CR 54:2761
34	D9S7	13	1	0.08	Pancreas	BJC 65:809
34	D957	12	0	. 0	Prostate	G 11:530

Chromosome 9 - q Arm

34	D9S7	13	2	0.15	Prostate	CSurveys 11:15
34	D957	11	- 2	0.16	Sarcoma	CR 52:2419
Unknown	D9S7	19	1	0.05	Testis	GCC 13:249
Unknown	D9S7	33	16	0.48	Testas	0 9:2245
34	D9S7	5	1	0.2	Uterus	GCC 9:119
Unknown	09511	252	153	0.61	Bladder	CR 53:1230
34	D957- D9S11-D9S13	252	149	0.59	Bladder	0 8:1083
34	D9S7- D9511-D9S13	252	149	0.59	Bladder	0 8:1083
Unknown	GSN- D9S:15-12	28	17	0.61	Bladder	CR 55:5213
Onknown	Unknown	20	1	0.05	Brain	CR 50:5784
21.1-22.2	Unknown	14	1	0.07	Brain	CR 54:1397
21,1-22.2	Unknown	19	0	0	Braio	CR 54:1397
Unknown	D9S6	13	0	0	Colon	CCG 48:167
Onknown	D95146	9	1	0.11	Endocrine	CR 56:599
Unknown	D9S160-180	44	26	0.59	Head&Neck	CR 54:4756
Unknown	D9S160-180	39	" 2	0.05	Head&Neck_	- CR 54:4756
Unknown	D9S:154-164-180	52	10	0.19	Leukemia	CR 55:5377
Unknown	Unknown	33	16.	0,48	Lung	CR 54:2322
Unknown	D9S15-10	26	14	0.54	Ovary	CR 53:2393
Unknown	Unknown	19	2 .	0.11	Prostate	PNAS 87:8751
SUM		6593	3076	0.47		

Chromosome 10 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
pter-pll.2	D10989	17	0	0	Uterus	CR 54:4294
Unknown	Unknown	38	15	0.39	Brain	CR 50:5784
Unknown	D1'09109	7.	0	O .	Brain	CR:53:2386
Unknown	D10S109	6	2	0.33	Brain	CR 53:2386
11.2	D105111.	9	-0	0	Brain	
11.2	D10S111	6	0	C	Brain	CR 53:2386
pter-pll.2	D10S89	8	0	0	Brain	CR 53:2386
pter-pl1.2	D10S89	16	1	0.06	Brain	CR 54:1397
pter-pll.2	D10989	6	1		Brain	CR 53:2386
pter-pll.2	D10S89	13	0	0	Brain	CR 54:1397
Unknown	FNRB- D10928	72	31	0.43	Brain	CR 56:164
pter-gl3	D10 S28	32	4	0.12	Breast	CR 50:7184
Unknown	~D10815	15	O	0	Breast	GCC 2:191
pter-q13	D10 S28	42	9	0.21	Cervix	CR 54:4481
Unknown	D108191	32	1	0.03	Cervix	CR 56:1972
13-12.2	D10524	4	0	0	Cervix	CR 54:4481
Unknown	010528	7	1	0.14	Cervix	GCC 9:119
Unknown	D10S249	14	1	0.07	Endocrine	CR 56:599
pter-pl1.2	D10S89	20	1	0.05	Endocrine	GCC 13:9
pTER-p13	D10S17	33	11	0.33	Esophageal	GCC 10:177
pTER-pl3	D10917	14	2	0.14	manus estados e estados comences o	CR 54:2996
Unknown	D10S226	11	0	0	Esophageal Head&Neck	CR 54:2336
Unknown	D108226	12	Ö	0	HeadsNeck	CR 54:4756
Unknown	D105249	22	5	0.23	····	CR 54:1152
pter-q13	D10 S28	31	3	0.1	Head&Necx	CR 51:5817
pter-gl3	D10 S28	34		0.09	Kidney	********************
pTER-pl3	D10517	Ti.	3 1	0.09	Kidney	CR 51:820
Unknown	D10S226	6	3		Kidney	CR 51:5817
Unknown	D108249-D108191	. 21	0	0.5	Kidney	GCC 12:76 PNAS 92:285
Unknown	D10S249-D10S191	5	0	0	Kidney	•••••••
pter-ql3	D10 S28	39	0	0	Kidney	PNAS 92:285 CR 51:89
pter-q13	D10 S28	35	5	0.14	Liver	
11-23.0	D10914	8	4	0.14	Lung	CR 52:2478
Unknown	D10S15	5	3		Melanoma	GCC 8:178
Unknown	D103226	23	4	0.6 0.17	Melanoma	GCC 8:178 CR 56:589
Unknown	D103220	14	and the second of the second o	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Melanoma	***************************************
Unknown	D10328	3	5	0.36	Melanoma	GCC 8:178
pter-pl1.2	D10533	······		0	Melanoma	GCC 8:178
pter-gl3	D10589	10 27	3	0.4	Melanoma	GCC 8:178
pter-gl3	D10 528 D10 S28			0.11	Ovary	CR 51:5118
Unknown	D10 528	35	5	0.14	Ovary	IJC 54:546
pter-al3	D10 S28	33 7	4	0.12	Ovary	CR 53:2393
pter-ql3	CONTRACTOR STATE OF THE PROPERTY OF THE PROPER		3	0.43	Pancreas	CR 54:2761
11-23.0	D10 928	1.9	4	0.21	Prostate	вли 73:390
13-pter	D10S14	11	3	0.27	Prostate	GCC 3:215
131 NP 21	D10917	1.8		0	Prostate	CSurveys 11

Chromosome 10 - p Arm

pTER-p13	D10S17	11	6	0.55	Prostate	G 11:530	
ptex-pl2	010517	11	- 6	0,55	Prostate	GCC 3:215	
pTER-p13	D10S17	18	0	o	Prostate	PNAS 87:875	
13-12.2	D10524	14	4	0:29	Prostate	GCC 3:215	
pter-pl2	D10S17	14	5	0.36	Sarcoma	CR 52:2419	
pter-q13	D10 S28	47	5	0.11	Testis	0 9 2245	
Unknown	D10528	14	4	0.29	Uterus	GCC 9:119	
pter-pl1.2	D10S89	17	-0	0	"Uterus"	CR 54: 4294	
SUM		980	172	0.18			

Chromosome 10 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
24-TER	PLAU	-5	0	0	Uterus -	CR 51:5632
Unknown	Unknown	37	14	0.38	Brain	CR 50:5784
12-gter	Onknown	12	0	-0	Brain	CR:54:1397
11.2	Unknown	12	0	0	Brain	CR 54:1397
11.2	Unknown	17	2	0.12	Brain	CR 54:1397-
12-qter	Unknown	15	1	0.07	Brain	CR 54:1397
Unknown	D109:25-22-1	64	21	0.33	Brain	
22-23	D10S1	5	0	0	Brain	CR 56:164
22-23	D1051	4	G	Ö	Brain	CR 48:5546
22-23	D10S1	10	10	1	******************************	CR 48:5546
Unknown	D108169	7	10	**************************************	Brain	CR 48:5546
Unknown	D105169	5		0	Brain	CR 53:2386
22-23	D103169	21	2	0.4	Brain	CR 53:2386
22-23			20	0,95	Brain	CR-48:5546
A CONTRACTOR OF THE PROPERTY AND ADDRESS OF THE PARTY OF	D10S4	6	0	0	Brain	CR 48:5546
22-23	D1054	11	0	. 0	Brain	CR 48:5546
24-TER	PLAU	10	0	0	Brain	CR 48:5546
74-TER	PLAU	5,	. 0	. 0	Brain +	CR 48:5546
24-TER	PLAU	14	14	1	Brain	CR 48:5546
22-23	D1051	18	2	0.11	Breast	CR"53:4356
26	D10S25	6	2	0.33	Breast	CR 53:3804
26	D10S25	23	2	0.09	Breast	CR 50:7184
26	D10S25	30	5	0.17	Breast	GCC 2:191
22-23	D1054	18	4	0.22	Breast	GCC 2:191
Unknown	D10S205	32	4	0.12	Cervix	CR 56:197
26	D10525	32	9	0.28	Cervix	CR 54:4481
26	D10S25	8	2	0.25	Cervix	GCC 9:119
11	D10S30	8	.2	0.25	Cervix	GCC 9:119
21.1	D10S5	17	1	0.06	Cervix	CR 54:4481
24-TER	PLAU	4	<u>-</u>	0,25	Cervix	CR 49:3598
24-TER	PLAU	6	0	0	Colon	IJC 53:382
Unknown	D105187	22	2	0.09	TOTAL SECTION AND DESCRIPTION OF THE PERSON ASSESSMENT OF THE PERSON AS	AND DESCRIPTION OF THE PROPERTY OF THE PROPERT
26	D10S25	25	4	0.16	Endocrine	***************************************
26	D10S25	36	6	THE RESIDENCE OF THE PROPERTY	Esophageal	CR 54:2996
26	D10525	17	***************************************	0.17	Esophageal	GCC 10:177
Unknown	D10323	12	0	0	Esophageal	CR 51:2113
Unknown	*******************************	*****	3	0.25	Head&Neck_	CR 54:4756
	D10S185	21	0	0	Head&Neck	CR 54:4756
Unknown	D10S221	. 24	5	0.21	***************************************	CR 54:1152
22-25	D10S13	32	9	0.28	Kidney	CR 51:5817
21	D10S14	17	5	-0.29	Kidney	CR 51:5817
Unknown	D10S185	6	3	0.5	Kidney	GCC 12:76
21-TER	D10520	25	. 8	0,32	Kidney	CR 51:5817
\$1,0000 \$200 \$500 \$00 PERSONS \$100 PERSONS FOR \$100 PERSO	105212-D105190		1	0.05	Kidney	PNAS 92:2854
Unknown [010S212-D10S190	5	0	0	Kidney	PNAS 92:2854
21	D10S22	10	3	0.3	Kidnev	CR 51:5817
21	D10523	15	3	0.2	Kidnev	CR 51:5817
26	D10S25	30	16	0.33	Kidnev	CR 51:5817
						3 31.301.

Chromosome 10 - q Arm

26	D10S25	21	2	0.29	Kidney	OD E3 000
22-25	D10S27	26	3	0.12	********************	CR 51:820
11	-	13	2		Kidney	CR 51:5817
26	D10536	27	5	0.15	<u>Kidney</u>	CR 51:5817
Unknown	D105201	19	3	0.19	Kidney	CR 51:5817
Unknown	Unknown	16		0,05	Leukemia	CR. 55:5377
22-23	DIOSI		0	0	Liver	CR 51:89
26	D1031	. <u>, 3</u> 24		0,33	Liver	CCG 48:72
Unknown	D10526	***************************************	6	0.25	Liver	CR 51:89
24-TER	***************	24	. 6	0.25	Liver	CR 51:89
	PLAU	20	0	0	Liver	JJCR 81:108
26	D10525.	25	5	0.2	Lung ·	CR 52:2478
Unknown	ATC	9	4	0.44	Melanoma	CR 54:3111
**************************************	CHLC.GGAA2F11	14	6	0.43	Melanoma	CR 54:3111
Unknown	D10S108	5	1	0.2	Melanoma	CR 54:3111
Unknown	-D10S110	4	- 2	0.5	Melanoma	CR 54:3111
Unknown	D10S168	8	5	0.62	Melanoma	CR 54:3111
Unknown	D108169	- 8	1	<pre>< 0.12</pre>	Melanoma	CR 54:3111
Unknown	D10S185	29	9	0.31	Melanoma	CR 56:589
Unknown	D10S187	12	. 3	0.25	Melanoma	CR 54:3111
21-22	D10S19	8	3	0.38	Melanoma	GCC 8:178
21-TER	D10S20	4	3	0.75	Melanoma	GCC 8:178
Unknown	D10S221	12	4	0.33	Melanoma	CR 54:3111
26	D10536	9	4	0.44	Melanoma	GCC 8:178
Unknown	D10S610	9	4	0.44	Melanoma	CR 54:3111
Unknown	D10588	- 6	3			CR 54:3111
	***************************************		3	0.5	Melanoma	
24-TER	PLAU	5	0	0.5	Melancma Neuroblast	**************************************
	PLAU	5	0	0	***************************************	om CR 49:1095
Unknown	PLAU D10S1-20	5 19		0	Neuroblast	**************************************
Unknown Unknown	PLAU D1051-20 D105173	5 19 16	0 2 3	0 0.11 0.19	Neuroblast a	om CR 49:1095 CR 53:2393 BJC 69:429
Unknown Unknown 26	PLAU D1051-20 D105173 D10525	5 19	0	0.11	Neuroblast a Ovary	om CR 49:1095 CR 53:2393
Unknown Unknown 26 26	PLAU D10S1=20 D10S173 D10S25 D10S25	5 19 16 34 24	0 2 3 4 5	0 0.11 0.19	Neuroblast a Ov ary Ovary	om CR 49:1095 CR 53:2393 BJC 69:429
Unknown Unknown 26 26 26	PLAU D10S1=20 D10S173 D10S25 D10S25 D10S25	5 19 16 34 24	0 2 3 4 5	0.11 0.19 0.12	Neuroblast a Ovary Ovary Ovary	om CR 49:1095 CR 53:2393 BJC 69:429 LJC 54:546
Unknown Unknown 26 26 26 Unknown	PLAU D10S1-20 D10S173 D10S25 D10S25 D10S25 Unknown	5 19 16 34 24 	0 2 3 4 5 0	0.11 0.19 0.12 0.21	Neuroblast a Ovary: Ovary Ovary Ovary	OR 49:1095 CR 53:2399 BJC 69:429 IJC 54:546 CR 51:5118
Unknown Unknown 26 26 26 Unknown 22-23	PLAU D10S1=20 D10S173 D10S25 D10S25 D10S25 Unknown D10S1	5 19 16 34 24	0 2 3 4 5	0 0.11 0.19 0.12 0.21	Neuroblast a Ovary Ovary Ovary Ovary Pancreas	OR CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761
Unknown Unknown 25 26 26 Unknown 22=23 21-22	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S1 D10S19	5 19 16 34 24 4 24 24	0 2 3 4 5 0 7	0.11 0.19 0.12 0.21 0.21	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate	OR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15
Unknown Unknown 26 26 26 Unknown 22=23 21-22 21-22	PLAU D10S1-20 D10S173 D10S25 D10S25 D10S25 Unknown D10S1 D10S19 D10S19	5 19 16 34 24 .4 24 2 8	0 2 3 4 5 0 7	0.11 0.19 0.12 0.21 0.29	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate Prostate	OR CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15 GCC 3:215
Unknown Unknown 26 26 26 Unknown 22-23 21-22 21-TER	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S19 D10S19 D10S20	5 19 16 34 24 4 24 2 8 7	0 2 3 4 5 0 7 7	0.11 0.19 0.12 0.21 0.29 0.29	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate Prostate	Om CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15 GCC 3:215 GCC 3:215
Unknown Unknown 26 26 26 Unknown 22=23 21-22 21-TER 26	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S19 D10S19 D10S20 D10S25	5 19 16 34 24 .4 24 2 8	0 2 3 3 4 4 5 5 0 0 7 7 0 0 1 D D	0.11 0.19 0.12 0.21 0.29 0.12	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate Prostate Prostate	Om CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15 GCC 3:215 GCC 3:215 GCC 11:119
Unknown Unknown 26 26 26 Unknown 22°23 21-22 21-7ER 26 26	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S19 D10S19 D10S20 D10S25 D10S25 D10S20	5 19 16 34 24 4 24 2 8 7	0 2 3 4 5 0 7 7 0 1 0 2 2	0 0.11 0.19 0.12 0.21 0 0.29 0 0.12 0	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate Prostate Prostate Prostate Prostate	Om CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15 GCC 3:215 GCC 11:119 GCC 3:215 GCC 11:119 GCC 11:530
Unknown Unknown 25 26 26 Unknown 22=23 21-22 21-TER 26 26 26	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S19 D10S19 D10S20 D10S25	5 19 16 34 24 .4 .24 .2 8 .7 .8	0 2 3 4 5 0 7 0 1 0 2 2	0 0 11 0 .19 0 .21 0 0 .29 0 0 .12 0 0 .25 0 .38	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate Prostate Prostate Prostate Prostate Prostate	Om CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15 GCC 3:215 GCC 3:215 GCC 11:119 GCC 3:215
Unknown Unknown 26 26 26 Unknown 22-23 21-22 21-TER 26 26 Unknown	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S19 D10S19 D10S19 D10S20 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25	5 19 16 34 24 4 24 2 8 7 8 8 13 13 9	0 2 3 4 5 0 7 7 0 1 0 2 2	0 0 11 0 . 19 0 . 21 0 0 . 29 0 0 . 12 0 0 . 25 0 . 38 0 . 31	Neuroblast a Ovary Ovary Ovary Pancreas Prostate Prostate Prostate Prostate Prostate Prostate Prostate	Om CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15 GCC 3:215 GCC 11:119 GCC 3:215 GCC 11:119 GCC 11:530
Unknown Unknown 25 26 26 Unknown 22=23 21-22 21-TER 26 26 26	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S19 D10S19 D10S20 D10S25 D10S25 D10S25 D10S25 D10S25	5 19 16 34 24 4 24 2 8 7 8 8 13	0 2 3 4 5 0 7 0 1 0 2 2 3	0 0.11 0.19 0.12 0.21 0 0.29 0 0.12 0 0.25 0.38 0.31	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate	Om CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15 GCC 3:215 GCC 3:215 GCC 11:119 G 11:530 GCC 3:215 GCC 3:215 GCC 3:215
Unknown Unknown 26 26 26 Unknown 22-23 21-22 21-TER 26 26 Unknown 22-23 26	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S19 D10S19 D10S19 D10S20 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25	5 19 16 34 24 4 24 2 8 7 8 8 13 13 9	0 2 3 4 5 0 7 0 1 0 2 3 4 4 2	0 0 11 0 19 0 19 0 29 0 0 12 0 25 0 31 0 22	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate	Om CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15 GCC 3:215 GCC 3:215 GCC 11:119 G 11:530 GCC 3:215 GCC 3:215 GCC 3:215
Unknown Unknown 29 26 26 26 Unknown 22-23 21-22 21-7ER 26 26 26 Unknown 22-23	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S19 D10S19 D10S20 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25 D10S26 D10S26	5 19 16 34 24 4 24 2 8 7 8 8 13 13 9	0 2 3 4 5 0 7 0 1 0 2 3 4 4	0 0.11 0.19 0.12 0.21 0 0.29 0 0.12 0 0.25 0.38 0.31 0.22 0.22	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate	Om CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15 GCC 3:215 GCC 3:215 GCC 11:119 G 11:530 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215
Unknown Unknown 25 26 26 26 Unknown 22-23 21-22 21-22 21-TER 26 26 Unknown 22-23 26 24-TER	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S19 D10S19 D10S20 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25 D10S26 D10S26 D10S20	5 19 16 34 24 4 24 2 8 7 8 8 13 13 9 10 19	0 2 3 4 5 0 7 0 1 0 2 3 4 4 2	0 0 11 0 . 19 0 . 21 0 0 0 . 29 0 0 . 25 0 . 38 0 . 31 0 . 22 0 . 2 1 0 . 4 2	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate	Om CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15 GCC 3:215 GCC 3:215 GCC 11:119 G 11:530 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215
Unknown Unknown 26 26 26 Unknown 22°23 21°22 21°7ER 26 26 Unknown 22°23 26 26 Unknown	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S19 D10S19 D10S20 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25 D10S26 D10S4 D10S90 OAT	5 19 16 34 24 4 24 2 8 7 8 8 13 13 9 10 19 25	0 2 3 4 5 0 7 0 1 0 2 3 4 4 4 2 1 8	0.11 0.19 0.12 0.21 0.29 0.12 0.12 0.25 0.38 0.31 0.22 0.12 0.22 0.31	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate	Om CR 49:1095 CR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 CR 54:2761 CSurveys 11:15 GCC 3:215 GCC 3:215 GCC 11:119 G 11:530 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215
Unknown Unknown 25 26 26 26 Unknown 22-23 21-22 21-22 21-TER 26 26 Unknown 22-23 26 24-TER	PLAU D10S1-20 D10S173 D10S25 D10S25 Unknown D10S1 D10S19 D10S19 D10S20 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25 D10S25 D10S26 D10S4 D10S90 QAT**	5 19 16 34 24 4 24 2 8 7 8 8 13 13 9 10 19 25 9	0 2 3 4 5 0 7 0 1 0 2 3 4 4 4 2 1 8 7 2 2	0.11 0.19 0.21 0.21 0.29 0.12 0.25 0.38 0.31 0.22 0.12 0.22 0.10 0.22	Neuroblast a Ovary Ovary Ovary Ovary Pancreas Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate	Om CR 49:1095 GR 53:2393 BJC 69:429 IJC 54:546 CR 51:5118 GR 54:2761 CSurveys 11:15 GCC 3:215 GCC 3:215 GCC 11:119 G 11:530 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215 GCC 3:215

Chromosome 10 - q Arm

Unknown	D10S26	20	0	0	Stomach	CR 51:2926
26	D10S25	34	9	0.26	Testis	0 9:2245
11.2	PTC	1	0	0	Testis	CCG 52:72
11.2	PTC	2	1	0.5	Testis	CCG 52:72
11,2	PTC	1	0	0	Testia -	CCG 57:72
Unknown	D10S173	16	1	0.06	Uterus	CR 54:4294
25	D10525	14	6	0.43	Uterus-	GCC 9:119
11	D10S30	12	3	0.25	Uterus	GCC 9:119
24-TER	PLAU	- 5	0	0	Oterus	CR 51:5632
SUM		1509	351	0.23		

Chromosome 11 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
Gnknown	RRAS1-D11912	17	77	0.41	Bladder	CR-51:5405
15.5	HRAS	7	2	0.29	Brain	CR 49:6572
15.5	RRAS	30	3	0.1	Breast	GCC 4:113
15.5	HRAS	24	3	0.12	Breast	CR 53:4486
15:5	HRAS	5	0	0	Breast	GCC:2:191
15.5	HRAS	68	21	0.31	Breast	GCC 12:304
15.5	HRAS.	30	8 .	0.27	Breast	IJC:53:11
15.5	HRAS	29	5	0.17	Breast	JJCR 84:11
15.5	HRAS	7	1	0.14	Breast	CR 53:3804
15.5	HRAS	33	1	0.03	Breast	CR 53:4356
15.5	BRAS	37	7	0:19	Breast	GE-5:5540
15.5	HRAS	6	0	0	Cervix	CR 49:3598
15.5	<u> </u>	18	-6	0.3394	Cervix	PNA9 91 69
15.5	HRAS	15	1	0.07	Cervix	BJC 67:71
15.5	RPAS	10	0	9 0	Colon	N=331:233
15.5	HRAS	16	0	0	Colon	CCG 48:167
15.5	HRAS	9	0	0	Colon	N 3319273
15.5	HRAS	9	1	0.11	Esophageal	CR 51:2113
15.5	RRAS	. 21	4	0.19	Esophageal	GCC 10:177
15.5	HRAS	20	8	0.4	Esophageal	CR 54:2996
15,5	HRAS	12	1	0.08	Head&Neck	CR 52:1494
15.5 15.5	HRAS	3	0	0	Kidney	CMB 38:59
15.5	RRAS	14	1	0.07	Kidney	CR 51:1071
15.5	HRAS	5	0	0	Kidney	CMB 38:59
15.5	HRAS HRAS	13	4	0.31	Leukemia	B 75:819
15.5	HRAS	5 3	0	0	Liver	JJCR 81:10
15.5	HRAS		***************************************	. 0	Liver	BJC 67:100
15.5	HRAS	13 4	0 9	0	Liver	GCC 1:312
15.5	HRAS	10	y 5	0	Liver	PNAS_86188
15.5	HRAS	5	0	0.5	Liver	CCG 48:72
15.5	HRAS	47	7	0.15	Liver	BJC 64:108
15.5	HRAS	39		0.15	Lung Lung	GCC 10:183 CR 54:1145
15.5	HRAS	13	5	0.38	Lung	PN 86:5099
15.5	RRAS	13	6	0.46		PN 91:5513
15.5	HRAS	2	1	0.5	Lung	PN 91:5513
15.5	HRAS	12	6	0.5	Lung	PN 86:5099
15.5	HRAS	7	1	0.14	Lunc	NEJ 317:11
15.5	HRAS	- 5	2	0.4	Lung	PN 86:5099
15.5	HRAS	13	3	0.23	Lung	PN 84:9252
15.5	HRAS	6	2	0.33	Lung	PN 91:5513
15.5	HRAS	4	0	0	Neuroblastor	***************************************
		(A)			a	
15,5	HRAS	. 25	10	0.4	Ovary	GO 47:137
15.5	HRAS	15	4	0.27	Ovary	GO 55:245
15.5	RRAS	11	5	0.45	Ovary.	CR 50:2724

Chromosome 11 - p Arm

15.5	HRAS	11	2	0.18	Ovary	T3C 54.546
15.5	HRAS	27	12	0.44	Ovary	IJC 54:546
15.5	HRAS	10	5	0.5	Ovary	C 72 2423
15.5	BRAS	13	2	0.15	Cvary	CR 49:1220
15.5	HRAS	19	9	0.47	Ovary	BJC 67:268
15.5	-HRAS	5	7	0.4	**************************************	PRJ 66:103
15.5	HRAS	20	7	0.35	Pancreas	3JC 65:809
15.5	BRAS	15	••••••	0.33	Pediatric	CR 50:3279
15.5	HRAS	9	0	0	Pedlatric	BG 97:163
15.5	HRAS	11		0.45	Prostate	GCC 11:119
15.5	HRAS	11	5		Sarcoma	
15.5	BRAS	9	٥	0.45	Sarcoma	CR 52:2419
15.5	HRAS	28	1		<u>Stomach</u>	CR 48:2988
155	HRAS	- 19	7	0.04	Stomach	CR 51:2926
15.5	HRAS	6	0	0.37	Stomach	HG 92:244
15.5	BRAS	15	7	0	Stomach	HG 89:445
15.5	HRAS	5		0.47	Testis	GCC 93153
15.5	HRAS	12	2	0.4	Testis	CCG 52:72
15.5	HRAS			0.25	Testis	GCC 9:153
15.5	ERAS	13	5	0.38	Testis	G 5:134
15.5			3	0.16	Ipstis	JU 153±168
15.5	HRAS	15	0	0	Testis	GCC 13:249
15.5	HRAS	15	5	0.33	Testis	GCC_7:85
	HRAS	3	1 1	0.33	Testis	CCG 52:72
15.5	BRAS	3	1	0.33	Testis	CCG 52:72
15.5	HRAS	9	1	0.11	Uterus	CR 51:5632
15.5	IGF2	7	2	0.29	Bladder	HG 91:455
15.5	IGF2	15	1	0.07	Breast	GE 5:554
15.5	IGF2	. 13	- 3	0.23	Cervix	0.12:423
15.5	IGF2	1	0	0	Lung	PN 91:5513
15.5	' IGP2	1	0	0	Lung	PN 91:5513
15.5	IGF2	1	0	0	Lung	PN 91:5513
15.5	.IGF2	14	- 6	0.43	Overy	BRJ 66:103
15.5	IGF2	9	6	0.67	Testis	JU 153:168
15.5	MUC2	17	2	0.12	Testis	GCC 13:249
15.5	H19	14	2	0.14	Cervix	0 12:423
Unknown	D118922	46	8	0.17	Bead&Neck	CR.54: 4756
Unknown	D11S922	40	1	0.03	Head&Neck	CR 54:4756
Unknown	D11S922	6	L	0.17	Kidney	PNAS 92:28
Unknown	D115922	19	1	0.05	Kidnev	PNAS 92:28
Unknown	D118922	8	4	0.5	Pediatric	HG 97:163
Unknown	D115922	49	16	0.33	Stomach	CR 56:268
Unknown	D1151318	16	7	0.44	Pediatric	HG 97:163
Unknown	D11S1318	15	9	0.6	Stomach	CR 56:268
15.5	INS	31	3	0.8	Breast	CR 50:7184
15.5	INS	23	4	0.17	Breast	GCC 2:191
15.5	INS	31	3	0.17	Breast	CR 5027184
		***************************************			presst.	CK JUL 1104

Chromosome 11 - p Arm

15.5	INS	3	•	_		
15.5	enī	3	0	0	Cervix	CR 49:3598
15.5	INS	15			Ceraix	CR/ 49 (3598)
15.5	INS	15	3	0.2	Colon	IJC 53:382
15.5	INS	8			Colon -	LUC (53:382
15.5	INS	8	2	0.25	Endocrine	CR 51:1154
15.5	INS	7		. 0.23	-Kidney	(ext \$5(23)0)
15.5	INS	21	0	0	Kidney	CMB 38:59
15.5	INS	7	3		Kidnev	CR/51:1071
15.5	INS	22	0 5	0	Kidney	CMB 38:59
15.5	INS	6			Kidney	CR.4511-820
15.5	INS	6	0	0	Liver	GCC 1:312
15.5	INS	9			Liver	CR:51:4363
15.5	INS	71	0	0	Liver	JJCR 81:10
15.5	INS			/(0,27		GR 51(6)9)
15.5	INS	10	2	0.2	Liver	CCG 48:72
15.5	INS	10		The second secon	Long	PN×86:5099
15.5	INS	5 14	1	0.2	Lung	PN 86:5099
15.5	INS	The second secon			Lung	FN:86:5099
15.5	INS	33 8	12	0.36	Lung	GCC 10:183
15.5	INS			0.12	Long.	PN:91:5513
15.5	INS	2 B	0	0	Lung	PN 91:5513
15.5	INS			0.12	Lung	PN 91:5513
15.5	INS	12	3	0.25	Lung	PN 84:9252
13.3	TNO	6	0	. 0	CONTRACTOR CONTRACTOR	om . CR 49:1095
15.5	INS	5	0	0	_ A .	an fa ann
15.5	INS	13	7	0.54	Ovary	CR 50:2724
15.5	INS	32	12	0.38	Overy	GQ 55:245
15.5	INS	27	7	0.26	Ovary	CR 51:5118
15.5	INS	20	7	0.35	Overv	BRJ 66:103
15.5	INS	23	10	0.33	Ovary Pediatric	CR 50:3279
15.5	INS	9	0	0	Stomach	CR 48:2988
15.5	INS	2	Ö	Ö	***********************	CR 52:3099
15.5	INS	15	4	0.27	Stomach Testis	GCC 7:96
15.5	INS	5		0.2	Testis	CCG 52:72
15.5	INS	2	0	0	Testis	CCG 52:72
15.5	INS	5	2	0.4	Testis	CCG 52:72
15.5	INS	15		0.2	Testis	G 5:134
15.5	INS	18	3	0.2	(000)	GCC 13:249
15.5	INS	3	0	0	<u>Testis</u>	CR 51:5632
15,5	TH	15	i i	0.57	Uterus	
15.5	TH	21	3	0.14	Brain Brain	CR 54:1397 CR 54:1397
15.5	TH	16	4	0.14		HMG 4:1889
15.5	TH	14	4	0.29	Breast Breast	CR 54:6270
15,5	TH	41	11	0.29	Breast	CR 53:4486
15.5	TH	14	1	0.07		BJC 67:71
15.5	TH	20	8	0.07	Cervix	
	-		•		Cervix	PNA9 91:69

Chromosome 11 - p Arm

15.5	TH	10	0	0	Kidney	CMB 38:59
155	278	8	- 0	0.00		CME 38 559
15.5	TH	8	1	0.12	Lung	PN 91:5513
15.5	78	10	0.7	T of	Lung	PN 913513
15.5	TH	2	0	0	Lung	PN 91:5513
15,5	THE SECTION	20/	7 7	0.35	Ovaro	GC 55.02
15.5	TH	23	9	0.39	Pediatric	HG 97:163
15.5	DRD4	7	1	0.14	Lung	***************************************
15.5	DRD4	3	0	0	Lung	PN 91:5513
Daknowa	0.015/15/1	13		0.46	Liver	
Unknown	D11S454	18	4	0.22	Lung	CR 52:2478
Unknown	D1/18/454	11	0		Overv	CR 51e558
15.5	D11S988	1	0	0	Lung	PN 91:5513
15.5	0119986	- 2	0		Lung	PN_91.5513
15.5	D115988	17	6	0.35	Pediatric	HG 97:163
15.5	DJ# \$988*#		E 12	0:71	Stomach	CR 56-258
15.5	D11S12	32	5	0.16	Breast	GE 5:554
15.5	DL1S17	3	1	0=33	Breast	GCC 2 A 9 1 1
15.5	D11S12	0	0	0	Cervix	CR 49:3598
15.5	D11S12 **	12	5	0.42	Cervix	CR 49:3598
15.5	D11S12	33	6	0.18	Esophagea.	
15.5	D11S12	15	3	0.2	Kidnev	CR.5121071
15.5	D11S12	11	8	0.73	Lung	PN 91:5513
15.5	D11S12	1	***************************************	1	Lung	PN 91:5513
15.5	D11S12	4	2	0.5	Lung	PN 91:5513
15.5	D11S12		. 2	0.5	Ovary	BRJ=662103
15.5	D11S12	3	1	0.33	Stomach	HG 89:445
_ 15.5	D11512	i	1	1-9	Testis	CCG 52172
15.5	D11S12	20	6	0.3	Testis	0 9:2245
15.5	D11S12		0	n	Testis	CCG 52:72
15.5	D11S12	8	3	0.38	Testis	JU 153:168
_ 15.5	P11912	5	1	0,2	Oterus	CR 51:5632
15.5-15.4	RRM1	42	7	0.17	Lung	GCC 10:183
15.5	HBB	27	9	0.33	Breast	CR 53:4486
15	HBG	6	0	0	Liver	PNAS 86:88
15.5,	HBB	2	0	0	Lung	PN 91:5513
15.5	HBB	4	0	0	Lung	PN 91:5513
15.5	HBB	6	Ö	0	Lung	PN 91:5513
15.5	HBG2	2	0	0	Lung	PN 86:5099
15.5	BBG2	8	4	0.5	Lung	PN-86:5099
15.5	HBG2	5	4	0.8	Lung	PN 86:5099
15.5	HBB	21	7	0.33	Pediatric	HG 97:163
15	GLOBIN	30	4	0.13	Breast	GE 5:554
15	GLOBIN	16	4	0.25	Drary	BRJ 663103
Unknown	GLOBIN	14	5	0.36	Ovary	BRJ 66:103
Enknown	GLOBIN	13	ž	0:15	Ovary	BRJ 66:103
					7.4	

Chromosome 11 - p Arm

19.5.5 0119932 1	15.5	D11S932	5	0	0	Lung	PN 91:5513
15.5	15.5	D11S932	9	1	0 11	Tuna	· · · · · · · · · · · · · · · · · · ·
Unknown D1153569 22 13 0.16 Stopach CR 55:258	15.5	D11S932	1	0		-	The state of the s
December December	Unknown	D113569	27	13	0.48		***************************************
Dec	Unknown	D11S569	24				
December Principal Princ	pter-15.4	PTH	11	1		***************	***************************************
PTE-15.4	pter-15.4			The second of th			and the state of t
Detail PTH	pter-15.4	PTH	7		**************************************	The second second	
Debt			8	· Accessor and the second consider.			
December 15.4 PTH 5	pter-15.4	PTH	7			***************************************	
Details PTB						The state of the s	The state of the s
December 15.4 PTH 7	pter-15.4	***************************************		····	***************************************		
PRIST-15.4 PRH 3 2 0.67 Teetis CCC 52.72 Peter-15.4 PTH 1 0 0 Testis CCG 52.72 Peter-15.4 PTH 1 0 0 Testis CCG 52.72 Peter-15.4 PTH 1 0 0 Testis CCG 52.72 Peter-15.4 PTH 15 6 0.4 Testis JU 153.168 13-15.1 D116419 14 6 0.43 Gyary BJG 69.429 Unknown D115902 28 8 0.29 Cervix PNAS 91.69 14-qtet D115899 6 0 0 0 0 Kidney GCC 12.76 15.5 D115861 21 5 0.24 Endocrine CR 56.599 15.5 D115861 21 5 0.24 Endocrine CR 56.599 15.5 D115861 7 0 0 Lung PN 91.5513 15.5 D115861 7 0 0 Lung PN 91.5513 15.5 D115860 27 9 0 0 Lung PN 91.5513 15.5 D115860 27 9 0 3 Breast CR 56.466 15.5 D115860 36 10 0.28 Breast CR 56.466 15.5 D115860 36 10 0.28 Breast CR 56.260 15.5 D115860 7 0 0 Lung PN 91.5513 15.5 D115860 7 0 0 Lung PN 91.5513 15.5 D115860 7 0 0 Lung PN 91.5513 15.5 D115860 7 0 0 Lung PN 91.5513 15.5 D115860 7 0 0 Lung PN 91.5513 15.5 D115860 7 0 0 Lung PN 91.5513 15.5 D115860 5 0 0 Lung PN 91.5513 15.5 D115860 5 0 0 Lung PN 91.5513 15.5 D115860 5 0 0 Lung PN 91.5513 15.5 D115860 6 6 0.38 Pediatric R6 97.163 15.5 D115860 6 6 0.38 Pediatric R6 97.163 15.5 D115860 6 6 0.38 Pediatric R6 97.163 15.5 D115860 6 6 0.36 Stomach CR 56.768 15.4 CALCA 6 0 0 Cervix Endocrine CR 56.751 15.4 CALCA 5 0 0 Cervix CR 58.152 15.4 CALCA 5 0 CALCA CALCA 5 0 CR 56.761 15.4 CALCA 7 0 0 Liver CR 51.152 15.4 CALCA 7 0 0 Liver CR 51.152 15.4 CALCA 3 0 Calca Calca Calca Calca Calca Calca Calca Calca Calca Calca Calca							
PTH	- Serioran conservation and the serior	**************************************				***************************************	
PTE	Carried Street, Street					-	
December 15	AND DESCRIPTION OF THE PARTY OF	· · · · · · · · · · · · · · · · · · ·					*****
13-15 D118419						***************************************	The state of the s
Unknown		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~				***************************************	***************************************
14-qter D11S899 23 4 0.17 Bead&Neck CR.56:1152 14-qter D11S899 6 0 0 0 Kidney GCC 12:76 15.5		The same of the sa			and the same of th		CONTRACTOR OF STREET,
14-qter	CONTRACTOR CONTRACTOR STANCES	CONTROL OF THE PROPERTY OF THE PARTY OF THE		***************************************	*****	****	**************************************
15.5							CR 54:1152
15.5 D11S861 1 0 0 0 Lung PN 91:5513 15.5 D11S861 7 0 0 0 Lung PN 91:5513 D0known D11S860 27 9 0.33 Breast CR 53:4486 15.5 D11S860 36 10 0.28 Breast Unknown D11S860 36 10 0.28 Breast Unknown D11S860 7 0 0 0 Lung PN 91:5513 D11S860 7 0 0 0 Lung PN 91:5513 15.5 D11S860 7 0 0 Lung PN 91:5513 15.5 D11S860 7 0 0 Lung PN 91:5513 15.5 D11S860 7 0 0 Lung PN 91:5513 15.5 D11S860 2 0 0 Lung PN 91:5513 15.5 D11S860 5 0 0 Lung PN 91:5513 15.5 D11S860 5 0 0 Lung PN 91:5513 15.5 D11S860 5 0 0 Lung PN 91:5513 15.5 D11S860 6 0 0 Lung PN 91:5513 15.5 D11S860 6 0 0 BLUNG PN 91:5513 15.5 D11S860 6 0 0 BLUNG PN 91:5513 15.5 D11S860 16 6 0 0 Bladder PN 91:5513 15.5 D11S860 16 6 0 0 Bladder PN 91:5513 15.4 CALCA 6 0 0 Bladder PG 91:455 15.4 CALCA 7 0 0 CRYIX BJC 67:71 15.4 CALCA 22 0 0 Freast GC 2:191 15.4 CALCA 5 0 0 Kidney CMB 38:59 15.4 CALCA 7 0 0 C Liver CCG 48:72 15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 7 0 0 0 Liver CCG 48:72 15.4 CALCA 7 0 0 0 Liver CCG 48:72 15.4 CALCA 7 0 0 0 Liver CCG 48:72 15.4 CALCA 7 0 0 0 Liver CCG 48:72		CONTRACTOR CONTRACTOR		-			GCC 12:76
15.5 Disser 9		A LONG TO SECURE AND A COLUMN TO SECURE AND A SECURE AND ASSESSMENT OF THE PARTY OF		- management		Endocrine	CR 56:599
15.5		10000000000000000000000000000000000000	1	0		Lung	PN 91:5513
Unknown Dis860 27 9 0.33 Breast CR:53:4466		*******************************			0	Lung	PN 91:5513
15.5	27.32.52.55364.655645.65564.6446.4644.4644.4644.	ANTONO CONTRACTOR CONT	7			Lung	PN 91:5513
15.5		Actual Control of the		<u>9</u>	0.33	Breast	CR 53:4486
15.5	***************************************	SOCIOCO POCOCOS SOCIONOS MANTENANDA DA ARRAMANA ARRAMANA ARRAMANA ARRAMANA ARRAMANA ARRAMANA ARRAMANA ARRAMANA			0.28	Breast	Unknown
15.5		The second secon		10	0.28	Breast	CR 54:6270
15.5	***************************************	CONSTRUCTION OF THE PROPERTY O	7			Lung	PN 91:5513
15.5			7	THE REAL PROPERTY AND ADDRESS OF THE PERSON.	0	Lung	PN 91:5513
15.5	42.1144.1144.4144.444.444.444.444.444.44	TO MORNO CONTROLLED CONTROL DE CONTROL				Lung	PN 91:5513
15.5 D11S860 2 0 0 Lung PN 91:5513		A CONTRACTOR OF THE PROPERTY O		0	0	Lung	PN 91:5513
15.5 D118860 16 6 0.38 Pediatric RG 97:163 15.5 D118860 44 16 0.36 Stomach CR 56:268 15.4 CALCA 6 0 0 Bladder RG 91:455 15.4 CALCA 17 1 0.06 Breast GC 2:191 15.4 CALCA 22 0 0 Breast GE 5:554 15.4 CALCA 22 0 0 Breast GE 5:554 15.4 CALCA 3 0 0 Kidney CMB 38:59 15.4 CALCA 5 0 0 Kidney CMB 38:59 15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 7 0 0 Liver CR 51:4367 15.4 CALCA 3 0 0 Liver GC 1:312		An and the common programmer and common and an annual section and	5	0	0	Lung	PN 91:5513
15.5 D11S860 64 16 D.36 Stomach CR 56:258 15.4 CALCA 6 0 0 Bladder HG 91:455 15.4 CALCA 17 1 0.06 Breast GCC 2:191 15.4 CALCA 22 0 0 Breast GE 5:554 15.4 CALCA 10 3 0:3 Cervix BJC 67:71 15.4 CALCA 5 0 0 Kidnev CMB 38:59 15.4 CALCA 5 0 0 Kidnev CMB 38:59 15.4 CALCA 7 0 0 Civer CCG 48:72 15.4 CALCA 7 0 0 Liver CR 51:4367 15.4 CALCA 3 0 0 Liver GR 51:4367 15.4 CALCA 3 0 0 Liver GCC 1:312 15.4 CALCA 3 0 0 Liver GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.4 CALCA 3 0 0 Civer GCC 1:312 15.5 CALCA 3 0 0 Civer GCC 1:312 15.6 CALCA 3 0 0 Civer GCC 1:312 15.6 CALCA 3 0 0 Civer CALCA CALCA CALCA 3 0 Civer CALCA	Commence of the Commence of th		. 2	0	0	Lung	PN 91:5513
15.4 CALCA 6 0 0 Bladder HG 91:455 15.4 CALCA 17 1 0.06 Breast GCC 2:191 15.4 CALCA 22 0 0 Breast GE 5:554 15.4 CALCA 10 3 0.3 Cervix BJC 67:71 15.4 CALCA 5 0 0 Kidnev CMB 38:59 15.4 CALCA 5 0 0 Kidnev CMB 38:59 15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 3 0 0 Liver GCC 1:312		MANAGEMENT COMPANY OF THE PROPERTY AND AN AN AN AN AN AN AN AN AN AN AN AN AN			0.38	Pediatric	HG 97:163
15.4 CALCA 6 0 0 Bladder HG 91:455 15.4 CALCA 17 1 0.06 Breast GCC 2:191 15.4 CALCA 22 0 0 Breast GE 5:554 15.4 CALCA 10 3 0.3 Cervix BJC 67:71 15.4 CALCA 5 0 0 Kidney CMB 38:59 15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 7 0 0 Liver CR 51:4367 15.4 CALCA 3 0 0 Liver GR 51:4367 15.4 CALCA 3 0 0 Liver GCC 1:312		D113860	. 64	1,6	0.36	Stomach	CR 56:268
15.4 CALCA 22 0 0 Breast GE 5:554 15.4 CALCA 10 3 0.3 Cervix BUC 67:71 15.4 CALCA 5 0 0 Kidney CMB 38:59 15.4 CALCA 4 0 0 Kidney CMB 38:59 15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 10 1 0:1 Liver CR 51:4367 15.4 CALCA 3 0 0 Liver GCC 1:312		CALCA				Bladder	
15.4 CALCA 22 0 0 Breast GE 5:554 15.4 CALCA 10 3 0.3 Cervix BJC 67:71 15.4 CALCA 5 0 0 Kidney CMB 38:59 15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 3 0 0 Liver GR 51:4367 15.4 CALCA 3 0 0 Liver GCC 1:312		CALCA	17	1	0.06	Breast	GCC 2:191
15:4 CALCA 10 3 0.3 CETYIX BJC 67:71 15:4 CALCA 5 0 0 0 Kidney CMB 38:59 15:4 CALCA 7 0 0 Liver CCG 48:72 15:4 CALCA 10 1 0.1 Liver CR 51:4367 15:4 CALCA 3 0 0 Liver CR 51:4367 15:4 CALCA 3 0 0 Liver GCC 1:312		CALCA	22		C		
15.4 CALCA 5 0 0 Kidney CMB 38:59 15.4 CALCA 7 0 0 Kidney CMB 38:59 15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 10 1 0.1 Liver CR 51:4367 15.4 CALCA 3 0 0 Liver GCC 1:312	15.4	CALCA	10	3	0.3	mekatracre asossisameessatametseksissi	BJC 67:71
15.4 CALCA 4 0 0 Kidney CMB 38:59 15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 10 1 0.1 Liver CR 51:4367 15.4 CALCA 3 0 0 Liver GCC 1:312	***************************************	CALCA	5			ALC: 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
15.4 CALCA 7 0 0 Liver CCG 48:72 15.4 CALCA 10 1 0.1 Liver CR 51:4367 15.4 CALCA 3 0 0 Liver GCC 1:312	15.4	CALCA	4	0			
15.4 CALCA 10 1 0.1 Liver CR 51:4367 15.4 CALCA 3 0 0 Liver GCC 1:312	**************************************		7	0			
15.4 CALCA 3 0 0 Liver GCC 1:312	15.4	CALCA	10	1		****	
22.02		CALCA				mana manananan manan manan manan manan manan manan manan manan manan manan manan manan manan manan manan manan	
	15.4	CALCA	6	0	0	Lung	PN 86:5099

Chromosome 11 - p Arm

15.4	CALCA	6	1	0.17	Luna	PN 91:5513
15.4	CYTCY	6	7	0.33	Lung	PN 86:5099
15.4	CALCA	2	0	0	Lung	PN 86:5099
15,4	CALCA *	3	1	0:33		PN 91:5513
15.4	CALCA	10	3	0.3	Ovary	C 72:2423
15.4	CALCA	15	6	0.4	Ovary	BRJ 66:103
15.4	CALCA	7	0	0	Stomach	HG 89:445
15.4	CALCA	6	3	0.5	Testis	GCC 7296
Unknown	D11S929	33	3	0.09	Cervix	CR 56:197
Unknown	0115929	17	4	0.24	Redistric	HG 97:163
13	D11S323	3	1	0.33	Lung	PN 91:5513
13	D11S323	3	1	0.33	Lung	PN 9135513
13	D115907	16	3	0.19	Endocrine	CR 56:599
13	0119907	14	1	0.07	Head&Neck	CR 54:1152
13	D11S907	1	0	0	Kidney	GCC 12:76
.13	D11516	17	4	*******	Cervix	PNAS 91:69
13	D11S16	30	4	0.13	Colon	IJC 53:382
13	D11516	5	0	Ö	Kidney	CMB 38:59
13	D11S16	4	0	0	Kidney	CMB 38:59
13	D11S16	6	0	Ç	Liver	GCC 1:312
13	D11516	7	2	0.29	Lung	PN 91:5513
13	D11S16	1	1	1	Lung	PN 91:5513
13	D11S16	10	7	- 0.7	Lung	PN 91:5513
13	011516	25	7	0.08	OverA	IJC 54:546
13	D11S16	23	6	0.26	Ovary	BRJ 66:103
13.	D11516	7	q	0.57	Testis	JU 153:168
13	D11S16	12	3	0.25	Testis	GCC 9:153
13	D11916	12	5	0.42	Testis	GCC 7:196
13	D11S16	5	2	0.4	Testis	GCC 9:153
13	D11S16	13	1	0.08	Uterus	CR 51:5632
13	D11S151	4	0	0	Lung	PN 91:5513
13	D118151	1	O	Ŏ.	Lung	PN 91:5513
13	D115151	3	0	0	Lung	PN 91:5513
13	D115151	11	3	0.27	Pediatric	CR 50:3279
13	D11S151	1	0	0	Testis	GCC 9:153
13	D118151	4	ō	0	Testis.	GCC 9:153
13	CAT	18	13	0.72	Bladder	HG 91:455
1,3	CAT	3	0	Ö	Kidney	CMB 38:59
13	CAT	16	2	0.12	Kidney	CR 51:1071
13	CAT	6	1	0.17	Kidney	CMB 38:59
13	CAT	7	0	0	Liver	CCG 48:72
12	CAT	6	Ö	. 0	Liver	GCC 1:312
13	CAT	8	3	0.38	Lung	PN 86:5099
13	CAT	2	o .	0.30	Lung	PN 86:5099
13	CAT	40	6	0.15	Lung	GCC 10:183
13	CAT	7	i	0.14	Lung	PN 8615099
					TANK TO THE PARTY OF THE PARTY	FN:0013U37)

Chromosome 11 - p Arm

13	CAT	2	1	0.5	Lung	DN 01.5512
13	CAT	7	0	0	Lung	PN 91:5513
13	CAT	10	0	0	Ovarv	EN 91 (5513)
13	CAT	24	6	0.25	Ovary	IJC 54:546
13	CAT	14	2	0.14	Pediatric	BRJ 66;103
13	CAT	4	1	0.25		CR 50:3279
13	CAT	12	5	0.42	Stomach	PG 89:445
13	CAT	i	o .	0.42	Testis	JU 153:168
13	CAT	3	1	0.33	Testis	CCG/52:72
13	CAT	1	0	0.33	Testis	CCG 52:72
13	D11S325	3	0	0	Testis	CCG 52:72
13	D115325	5	0	0	Lung	PN 91:5513
13	D11S325	6	2	0.33	Lung	PN 9135513
13	D115325	6	1	0.33	Testis	GCC 9:153
13	D11S325	16	2	The state of the s	Testis	GCC 9:153
13	D4S414	15	5	0.12	Testis	GCC 7:96
13	D4S414	2	1	0,33	Bladder	RG 91: 455
13	D45414	4	1	0.5	Lung	CR 54:5643
13	D4S414	21	4	0.25	Lung	CR 54:5643
13	B-FSE	*****	6	0.19	Lung	CR 54:5643
13	B-FSH	16 4		0.38	Bladder	BG:91:455
13	B-FSH	46	0 9	0	Cervix	BJC 67:71
13	B-FSH		THE STATE OF THE PERSON ASSESSMENT	0.2	Lung	GCC 10:183
13	MANAGA MA	24 14	7 5	0.29	Ovary	BRJ 66:103
13	B-FSH	**************************************		0.36	Pediatric	CR 50: 3279
13	B-FSH	7 25	1 D	0.14	Stomach	HG 89:445
13	0118905			0	Esophageal	IJC 69:1
11.2-12	D11S905	18	4	0.22	Pediatric	HG 97:163
100000000000000000000000000000000000000	D113149	3	. 0	0	Endocrine	CR 51:1154
11.2-12 11.2-12	D115149	7 1	1	0.14	Lung	PN 91:5513
	D11S149	CALCOLOMO BOLLON TO SERVICE SONO SECURIO	0	0	Lung	PN 91:5513
11.2-12 12	D11S149	5	0	0	Lung	FN 91:5513
12	D115288	10	2	0,2	Cervix	_ PNAS 91:69
12	D11S1313	48	12	0.25	Lung	GCC 13:40
	D11S1313	48	12	0.25	Lung	GCC 13:40
Unknown	DllS:907-929	28	15	0.54	Bladder	CR 55:5213
Unknown	Unknown	14	3	0.21	Brain	CR-50:5784
15	Unknown	35	2	0.06	Breast	JNCI 84:50
Daknown	D11SS1318	18 ,	6	0.33	Breast	_HMG 4:1889
Unknown	D11SS1323	9	5	0.56	Breast	HMG 4:1889
Unknown	D11531338	9	5	0.56	Breast	EMG 4:1889
Unknown	D11SS1760	7	2	0.29	Breast	HMG 4:1889
11	D11S554	22	5	0.23	Cervix	BJC 71:814
Unknown	D11S740	5	0	0	Cervix	GCC 9:119
11	D118554	22	6	0.27	Endocrine	CR 56:599.
15.5	D11S576	25	0	С	Kidney	BJC 69:230
Daknown	D115:922-904	6	3	0.5	Kidney	GCC 12:76

Chromosome 11 - p Arm

Description	15.5	JW1-51	16	4	0.25	Kidnev	CR 51:1071
13	pter-pl3	D11S17	6	0	Ō		
13		****			0.09	Marie of the control	
15	STANDARD TO THE COST CONTRACT	D11s21	. 5	0	. 0	Liver	
15 15 15 15 15 15 15 15				1	0.12		
14	15.3-15.4	D1151243	57	14	0.25	Lung	***************************************
15.4-15.5		**************************************	57	17	0.3		the second second second second
11.2-12 DISIZEZ 54 13 0.24 Lung GCC 13:40 15.4-15.5 DISIZEZ 54 13 0.24 Lung GCC 13:40 15.4-15.5 DISIZEZ 59 12 0.31 Lung GCC 13:40 Vinknown HRAS-INS-HBG 1 1 Lung CR 50:2303 Unknown HRAS-INS-HBG 1 0 0 Lung CR 50:2303 Daknown BRAS-INS-HBG 1 0 0 Lung CR 50:2303 Daknown HRAS-INS-HBG 1 0 0 Lung CR 50:2303 Unknown HRAS-INS-HBG 1 0 0 Lung CR 50:2303 Unknown HRAS-INS-HBG 3 0 0 Lung CR 50:2303 Unknown HRAS-INS-HBG 3 0 0 Lung PN 91:5513 15.5 ST5 4 0 0 Lung PN 91:5513 15.5 ST5 1 0 Ung PN 91:5513 15.5 ST5 1 0 Ung PN 91:5513 Unknown Ullsi92-904 32 4 0.12 Melanoma CR 56:589 Unknown Unknown 1 2 0.18 Ovary IJC 52:575 15 Ulknown 5 1 0.2 Ovary OS:219 Unknown Unknown 5 1 0.2 Ovary OS:219 Unknown DILSI92-791 10 6 0.33 Ovary BJ 66:103 Unknown DILSI33 7 9 0.55 Ovary BJ 66:103 Unknown DILSI333 7 2 0.29 Pediatric HG 97:163 Unknown DILSI333 7 2 0.29 Pediatric HG 97:163 Unknown Unknown 1 0 0 Pancreas CR 54:2756 Unknown Ulknown 10 0 Prostate Surveys IJC 52:530 Unknown Ulknown 10 0 Prostate Surveys IJC 52:530 Unknown Ulknown 10 0 Prostate Surveys IJC 52:530 Unknown Ulknown 10 0 Prostate Surveys IJC 52:530 Unknown Ulknown 11 0 0 Prostate Surveys IJC 52:530 Unknown Ulknown 11 0 0 Prostate Surveys IJC 52:530 Unknown Ulknown 11 0 0 Prostate Surveys IJC 52:530 Unknown Ulknown IJC 0 0 Prostate Surveys IJC 52:530 Unknown Ulknown IJC 0 0 Prostate Surveys IJC 52:530 Unknown Ulknown IJC 0 0 Prostate Surveys IJC 52:530 Unknown Ulknown IJC 0 0 Prostate Surveys IJC 52:530 Unknown IJC 0 0 Prostate Surveys IJC 52:5	or constitution and the contract of the co	D11S1250	50	17	0.34	***************************************	
11.2-12	577400000000000000000000000000000000000	D1151251	66	21	0.32		
15.4-15.5 DIISI254 39 12 D.31 Lung GCC 13:40		D1151252	54	13	0.24	****	
Unknown HRAS-INS-HBG 1	15.4-15.5	D11S1254	39	12			the same of the same of the same of the same of
Unknown	Unknown	HRAS-INS-HEG	1	1	1		
Description BRAS-INS-HBC 1	Unknown	HRAS-INS-HBG	27	4	0.15		
Unknown	Onknown	BRAS-INS-HBG	1	-0	***************************************	****	
Darkown	Unknown	HRAS-INS-HBG	13	4	0.31		
15.5 ST5 4 0 0 0 Lung PN 91:5513 15.5 ST5 9 0 0 0 Lung PN 91:5513 15.5 ST5 9 0 0 0 Lung PN 91:5513 15.5 ST5 9 0 0 0 Lung PN 91:5513 15.6 Lung PN 91:5513 15.6 Lung PN 91:5513 15.6 Lung PN 91:5513 15.6 Lung PN 91:5513 15.7 Lung PN 91:5513 15.7 Lung PN 91:5513 16.7 Lung PN 91:5513 17.7 Lung PN 91:5513 18.7 Lung PN 91:5513 19.7 Lung PN 91:551 19.7 Lung PN 91:551 19.7 Lung PN 91:551 19.7 L		HRAS-INS-HEG	3	0	0	***************************************	-
15.5 S15 9		ST5	4	0	0		The state of the s
15.5 ST5 9 0 0 Lung PN 91:5513		375	1	0	0	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	***************************************
Unknown D115:922-904 32 4 0.12 Melanoma CR 55:588 Unknown Unknown 11 2 0.18 Ovary IJC 52:575 15 Unknown 5 1 0.12 Ovary 0.5:219 Unknown 9 4 0.44 Ovary 0.5:219 Unknown CALCA-HRASI-INS-PTH 17 9 0.53 Ovary GO 55:198 Dete-pl3 D11S17 17 6 0.35 Ovary BAJ 66:103 Unknown D11S1554-875-971 18 6 0.33 Ovary BAJ 67:193 Unknown PRAS-CAT-D11S16 34 12 0.35 Ovary CR 54:2761 Unknown PARC-CAT-D11S16 34 12 0.35 Ovary CR 54:2761 Unknown D11S13233 7 2 0.29 Pediatric HG 97:163 Unknown D11S31338 14 3 0.21 Pediatric HG 97:163 Unknown	***************************************	ST5		0	0		The same of the sa
Unknown	Unknown	D11S:922-904	32	4	0.12		COOCHER CONTRACTOR CON
15		Unknown		2			and the same of th
This This		Unknown	5	1		***************************************	
Distribution CALCA-HRASI-INS-PTH 17 9 0.53 Ovary Distribution Dis	15	Unknown	9	4	The second secon		
Discript	Unknown	CALCA-HRAS1-INS-PT	17	9	Contract Con	***************************************	MANAGER STANKES ASSESSMENT ASSESS
Biknown Dils:554-875-871 19 6 0.33 Ovary BUC 72:133 Unknown RAS-CAT-DILS:6 34 12 0.35 Ovary CR 53:2393 15.5 Unknown 3 0 0 Pancreas CR 54:2761 Unknown Dils:323 7 2 0.29 Pediatric HG 97:163 Unknown Dils:338 14 3 0.21 Pediatric HG 97:163 Unknown Dils:338 14 3 0.21 Pediatric HG 97:163 Unknown Dils:937 10 1 0.1 Pediatric HG 97:163 Unknown Unknown 11 0 0 Prostate CSurveys 1 Unknown Unknown 11 0 0 Prostate CSurveys 1 Unknown Unknown 10 0 0 Prostate CSurveys 1 Unknown CALCA-HRASI-HBG2 15 0 0 Prostate G 11:530 Unknown Dils:2351 40 16 0.4 Stomach GR 56:268 Unknown Dils:324 8 3 0.38 Testis GCC 9:153 Unknown Dils:324 7 3 0.43 Testis GCC 9:153 Unknown Dils:324 7 3 0.43 Testis GCC 9:153 Unknown Dils:324 7 3 0.43 Testis GCC 9:153 Unknown Dils:324 7 3 0.43 Testis GCC 9:153 Unknown Dils:324 7 3 0.27 Testis GCC 9:153 Unknown Dils:324 7 3 0.66 Testis GCC 9:153 Unknown Dils:417 11 3 0.27 Testis GCC 9:153 Unknown FSHB 4 0 0 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 7 2 0.29 Testis GCC 9:153 Unknown Dils:740 8 1 0.12 Uterus GCC 9:119 Unknown Dils:740 8 1 0.12 Uterus GCC 9:119 Unknown Dils:740 8 1 0.12 Uterus GCC 9:119 Unknown Dils:740 8 1 0.12 Uterus GCC 9:119 Unknown Dils:740 8 1 0.12 Uterus GCC 9:119 Unknown Dils:740 8 1 0.12 Uterus GCC 9:119 Unknown Dils:740 8 1 0.12 Uterus GCC 9:119 Unknown Dils:740 8 1 0.12 Uterus GCC 9:119 Unknown Dils:740 8 1 0.12 Uterus GCC 9:119 Unknown Dils:740 8 1 0.12 Uterus GCC 9:119 Unknown Dils:740 8 1 0.12 Uterus GCC 9:119 Unknown Dils:	pter-pl3	D11S17		6			ALCOHOLOGICA CONTRACTOR CONTRACTO
Number N	Baknowa	D11S:554-875-871	18	6		SOMEONE WILLIAM STREET	A A MATCHING TO THE PARTY OF TH
15.5	27 SANGER COMMANDER STREET	RAS-CAT-D11S16	34	man an an an an an an an an an an an an a			NAMES AND ASSOCIATION OF THE PROPERTY.
Unknown D11S1323 7 2 0.29 Pediatric HG 97:163 Birknown D11S133B 14 3 0.21 Pediatric HG 97:163 Unknown D11S937 10 1 0.1 Pediatric HG 97:163 13 WT1 16 8 0.5 Pediatric HG 97:163 Unknown Unknown 11 0 0 Prostate CSurveys 1 Enknown Unknown 10 0 0 Prostate PNAS 87:87 Unknown Unknown 10 0 0 Prostate PNAS 87:87 Unknown Unknown 10 0 0 Prostate PNAS 87:87 Unknown D11S2351 40 16 0.4 Stomach CR 56:268 Unknown D11S324 8 3 0.38 Testis GCC 9:153 Unknown D11S417 11 3 0.27 Testis GCC 9:153 Unknown FSH	15.5	Unknown	3	Ö	*******************************	*****	***************************************
Binknown Dilsi338	Unknown	D11S1323	7		0.29		con contract company and the first contract of the contract of
Unknown D11S937 10 1 0.1 Pediatric HG 97:163 13 WT1 16 8 0.5 Pediatric HG 97:163 Unknown Unknown 11 0 0 Prostate CSurveys 1 Unknown Unknown 10 0 0 Prostate PNAS 87:87 Unknown CALCA-HRAS1-HBG2 15 0 0 Prostate G 11:530 Unknown D12S2351 40 16 0:4 Stomach CR 56:268 Unknown D11S324 8 3 0.38 Testis GCC 9:153 Unknown D11S417 11 3 0.27 Testis GCC 9:153 Unknown D11S417 1 3 0.16 Testis GCC 9:153 Unknown FSHB 4 0 0 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB	Onknown	D11S1338	14	3	0.21	*******************************	
13		D11S937				*****	and a service of the
Unknown Unknown 11 0 0 Prostate CSurveys 1 Unknown Unknown 10 0 0 Prostate PNAS 87:87 Unknown CALCA-HRAS1-HBG2 15 0 0 Prostate G 11:530 Unknown D12S2351 40 16 0:4 Stomach CR 56:268 Unknown D115324 8 3 0.38 Testis GCC 9:153 Unknown D11S417 11 3 0.43 Testis GCC 9:153 Unknown D11S417 11 3 0.27 Testis GCC 9:153 Unknown FSHB 4 0 0 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 7 2 0.29 Testis GCC 7:96 Unknown D115740	13	. WT1	16	8		***************************************	*****************************
Unknown Unknown 10 0 D Prostate PNAS 87:87 Unknown CALCA-HRAS1-HBG2 15 0 0 Prostate G 11:530 Unknown D12s2351 40 16 0:4 Stomach CR 56:268 Unknown D11s324 8 3 0.38 Testis GCC 9:153 Unknown D11s417 11 3 0.27 Testis GCC 9:153 Unknown D11s417 1 3 0.27 Testis GCC 9:153 Unknown FSHB 4 0 0 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 4 0 0 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 7 2 0.29 Testis GCC 7:96 Unknown D115740 8<	****************************	Unknown	11		0	Comment of the Commen	Contract of the contract of th
Unknown CALCA-HRAS1-HBG2 15 0 0 Prostate G 11:530 Unknown D12S2351 40 16 0:4 Stomach CR 56:268 Unknown D11S324 8 3 0.38 Testis GCC 9:153 Unknown D11S324 7 3 0.43 Testis GCC 9:153 Unknown D11S417 11 3 0.27 Testis GCC 9:153 Unknown FSHB 4 0 0 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 7 2 0.29 Testis GCC 7:96 13 WTI 10 5 0.5 Testis GCC 9:119 Unknown D11S740 8	Unknown	Unknown	10	0	0	***********************	encomponencia processo de la componencia della componencia della componencia della componencia della componencia della componencia della della componencia della componencia della componencia della componencia della componencia della componencia della componencia della componencia della componencia della componencia della componencia della componencia della componencia della componencia d
Unknown D13S2351 40 16 0.4 Stomach CR 56:268 Unknown D11S324 8 3 0.38 Testis GCC 9:153 Unknown D11S324 7 3 0.43 Testis GCC 9:153 Unknown D11S417 11 3 0.27 Testis GCC 9:153 Unknown D11S417 5 3 0.6 Testis GCC 9:153 Unknown FSHB 4 0 0 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 7 2 0.29 Testis GCC 7:96 13 WI1 10 5 0.5 Testis GCC 7:96 Unknown D11S740 8 1 0.12 Uterus GCC 9:119	Unknown	CALCA-HRAS1-HBG2	15	0			(((((((((((((((((((
Unknown D115324 8 3 0.38 Testis GCC 9:153 Unknown D115324 7 3 0.43 Testis GCC 9:153 Unknown D115417 11 3 0.27 Testis GCC 9:153 Unknown F5HB 4 0 0 Testis GCC 9:153 Unknown F5HB 8 3 0.38 Testis GCC 9:153 Unknown F5HB 7 2 0.38 Testis GCC 9:153 Unknown F5HB 7 2 0.29 Testis GCC 7:96 13 WT1 10 5 0.5 Testis GCC 7:96 Unknown D115740 8 1 0.12 Uterus GCC 9:119	Unknown	01182351	40	16	0.4	************	CONTRACTOR OF THE PROPERTY OF
Onknown D115324 7 3 0.43 Testis GCC 9:153 Unknown D115417 11 3 0.27 Testis GCC 9:153 Unknown D115417 5 3 0:6 Testis GCC 9:153 Unknown FSHB 4 0 0 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 7 2 0.29 Testis GCC 7:96 13 WT1 10 5 0.5 Testis GCC 7:96 Unknown D115740 8 1 0.12 Uterus GCC 9:119	Unknown	D115324		3		and were a construction of the second section (Contract of the State of the St
Unknown D11S417 11 3 0.27 Testis GCC 9:153 Unknown D11S417 5 3 0.16 Testis GCC 9:153 Unknown FSHB 4 0 0 Testis GCC 9:153 Unknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 7 2 0.29 Testis GCC 7:96 13 WTI 10 5 0.5 Testis GCC 7:96 Unknown D115740 8 1 0.12 Uterus GCC 9:119	Unknown	D115324	7	3.	0.43	Maria Concernation Service Agreement Agreement and Agreement Agree	
Unknown D118417 5 3 0.6 Testis GCC 9:153 Unknown FSHB 4 0 0 Testis GCC 9:153 GRknown FSHB 8 3 0.38 Testis GCC 9:153 Unknown FSHB 7 2 0.29 Testis GCC 7:96 13 WT1 10 5 0.5 Testis GCC 7:96 Unknown D115740 8 1 0.12 Uterus GCC 9:119		D11S417		3			
Unknown FSHB 4 0 0 Testis GCC 9:153 Grknown FSHB 8 3 0,38 Testis GCC 9:153 Unknown FSHB 7 2 0.29 Testis GCC 7:96 13 WT1 10 5 0.5 Testis GCC 7:96 Unknown D115740 8 1 0.12 Uterus GCC 9:119	Unknown	D115417	5			MCCCCCCAC TOTAL CONTRACTOR CONTRACTOR	AND AND DESCRIPTION OF A PARTY OF
Unknown FSHB 8 3 0,38 Testis GCC 9:153 Unknown FSHB 7 2 0.29 Testis GCC 7:96 13 WT1 10 5 0.5 Testis GCC 7:96 Unknown D115740 8 1 0.12 Uterus GCC 9:119	Unknown	FSHB	4	0			
Unknown FSHB 7 2 0.29 Testis GCC 7:96 13 NT1 10 5 0.5 Testis GCC 7:96 Unknown D11S740 8 1 0.12 Uterus GCC 9:119	Caknown	FSHB	. 8	3	•	***	
13 WII 10 5 0.5 Testis GCC 7:96 Unknown D115740 8 1 0.12 Uterus GCC 9:119	COMMON COMMON CONTRACTOR OF THE	FSHB		2			THE PROPERTY OF THE PARTY OF TH
Unknown D115740 8 1 0.12 Uterus GCC 9:119	2	WT1	10	5		COCCOMO COCCOMO CONTRACTOR AND AND AND AND AND AND AND AND AND AND	
	TOWNS AND ADDRESS OF THE PARTY	D115740		1		CONTRACTOR OF THE PARTY OF THE	
	13	WT1	24	0	0	***************************************	CR 54:4294

WO 98/41648

PCT/US98/05419

94 / 214

Chromosome 11 - p Arm

SUM

4917 1151 0.23

WO 98/41648

Chromosome 11 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
12-13.2	PYGM	12	5	0.42	Breast	CR 54:4586
12-13.3	PYGM-INT2	36	24	0.67	Breast	CR 55:467
12-13.2	PYGM	30	5	0.17	Cervix	PNAS 91:6953
12-13.2	PYGM	3	2	0.67	Endocrine	GCC 12:73
12-13.2	PYGM	16	- 6	0.38	Endocrine	****
12-13.2	PYGM	4	2	0.5		CR 56:599
12-13.2	PYGM	€2.	5	0.12	Endocrine	CR 51:1154
12-13.2	PYGM	15	2	0.13	Esophageal.	GCC 10:177
12-13.2	PYGM	.13	0		Kidney	CR 51:5817
12-13.2	PYGM	7	2	0	Prostate	G 11:530
12	CD20	12	-3	0.29	Stomach	HG 89:445
Unknown	PGA	11		0.25	Ovary	BJC 67:268
Unknown	PGA	-	0	0	Colon	CCG 48:167
Unknown		6-	1	0.17	Endocrine	CR 51:1154
****	PGA	15	2	0.13	Testis	GCC 7:96
Dnknown	PGA	15	2 .	0.13	Testis	LI 73:606
13	FGF3	40	4	0.1	Breast	CR 54:6270
13	FGF3	16	. 3	0.19	Ovary	BJC 67:258
13	D11S913	36	0	0	Esophageal	IJC 69:1
13,1	D11S97	25	7	0.28	Cervix	PNAS 91:6953
13.1	D11597	23	4	0.17	Testis	GCC 13:249
12-13.2	D115146	6	2	0.33	Endocrine	CR 51:1154
12-13.2	D11S146	15	1	0.07	Kidney	CR 51:5817
12-13.2	0115146	23	3	0.13	Liver	CR 51:89
12-13.2	D11S146	10	1	0.1	Ovarv	BJC 67:268
13	WT-1	14	7	0.5	Bladder	HG 91:455
13	WT-1	13	4	0.31	Breast	CR 54:6270
13	WT-1	20	6	0.3	Cervix	Carlo co commente an anni an a fan air a in
13	WT-1	52	5	0.1	Lung	PNAS 91:6953
13	WT-1	21	4	0.19	*** **********************************	GCC 10:183
13	WT-1	2	1	0.5	Lung	CR 54:5643
13	WT-1	4	0	0.5	Lung	CR 54:5643
13	WT-1	1	0	******************	Lung	PN 91:5513
13	wr-1	6	0	0 0	Lung	PN 91:5513
13	WT-1	4			Lung	PN 91:5513
13	INT2	22	1	0.25	Lung	CR 54:5643
13	INT2		<u>B</u>	0.36	Bladder	CR 55:5213
2.53.575.079.2.23.49.499.00000.ceo.c.o.	Section by an experience of the property of	3	0	0	Breast	CR 53:3804
13 13	INT2	.12	0	. 0	Breast	CR 50:7184
**********************	INT2	34	5	0.15	Breast	CR 53:4356
13	INT2	9	1	0.11	Cervix	GCC 9:119
13	INT2	22	1	0.05	Cervix	CR 54:4481
13	INT2	3	1	0.33	Cervix	CR 54:4481
13	INT2	15	0	0	Cervix	CR 49:3598
13	INT2	22	8	0.36	Cervix	PNAS 91:6953
13	INT2	22	7	0.32	Colon	GCC 6:45
13,	INT2	5	2	0.4	Endocrine	GCC 12:73
13	INT2	11	3	0.27	Endocrine	CR 51:1154
			-		2	J. J. 1134

Chromosome 11 - q Arm

: 13	INT2	g	0	٥	Esophageal	CR 51:2113
13	INT2	13	6	0.46	Head&Neck	CR 54:1152
13	INT2	9	3	0.33	Kidney	
13	INT2	9	3	0.33	Kidnev	CR 51:5817
13	INT2	4	1	0.25	Kidney	CR 51:1071
13	INT2	7	1	0.14	Liver	CR 51:4367
13	INT2	11	3	0.27	Lung	PNA9 86:5099
13	INT2	3	1	0.33	Lunc	PNAS 86:5099
13	INT2	11	2	0.18	Lung	PNAS 86:5099
13	INT2	24	3	0.12	Lung	CR 52:2478
13	INT2	6	0	0	Ovary	CR 50:2724
13	INT2	21	0	0	Ovary	IJC 54:546
13	INT2	19	1	-0.05	Overy	CR 51:5118
13	INT2	8	2	0.25	Stomach	HG 89:445
13	INT2	18	0	0.23	Stomach	CR 51:2926 -
13	INT2	11	1	0.09	Stomach	CR 48:2988
13	INT2	27	4	0.09	Testis	0 9:2245
13	INT2	4	2	0.5	Testis	0 9:2245
13	INT2	3	- 2	0.33	Testis	CCG 52:72
13	INT2	4	1			***************************************
13	INT2	īi.	1 2	0.25 0.18	Testis	CCG 52:72
13	INT2	<u> </u>	*******************************		Oterus	GCC 9:119
13.2-22	D11S141	4	1	0.2	Uterus	CR 51:5632
13	D11S534	23	6	0.26	Stomach	HG 89:445
13	D119534	13	4	0.31	Cervix	BJC 71:814
Unknown	D115534	······································		*************	Ovary	Unknown
processor recognization continues and	D118533	38	12	0.32	Cervix	PNAS 91:6953
Unknown Unknown	**********************	21		0.24	Endocrine	GCC 13:9
00010 00000000000000000000000000000000	D11S533	16	4	0.25	Ovary	GO 55:245
Unknown	D119911	23	3	0.13	Cervix	CR 56:197
23.3	D11S901	39	13	0.33	Breast	CR 54:4586
23.3	_D118901	33	11	0.33	Cervix	PNAS 91:6953
23.3	D115901	21	6	0.29	Stomach	CR 56:268
14-21	TYR	2	0	<u></u> 0	Lung	PN 91:5513
14-21	TYR	7	0	0	Lung	PN 91:5513
14-21	TYR		i	0.14	Lung	PN 91:5513
14-21	TYR	16	3	0.19	Ovary	BJC 67:268
14-21	TYR	3	2	0.67	9tomach_	HG 89:445
22-23	D11S923	36	2	0.06	Esophageal	IJC 69:1
22	D11935	28	7	0.25	Breast	CR 54:6270 ;
22	D11S35	34	12	0.35	Breast	CR 54:4586
22	D11S35	21	12	0.57	Cervix	PNAS 91:6953
22	D11S35	34	10	0.29	Stomach	CR 56:268
22	D11535	33	4	0.12	Uterus	CR 54:4294
22	STMY1	12	6	0.5	Colon	GCC 6:45
22	STMY1	.11	6	0.55	Ovary	BJC 67:268
22	STMY1	7	2	0.29	Stomach	HG 89:445

Chromosome 11 - q Arm

22-23.	DRD2	68	23	.0.34	Colon	BJC 70:395
Unknown	D11S1341	8	3	0.38	Stomach	CR 56:268
22.3-23.3	D115144	6	1	0.17	Brain	CR 49:6572
22.3-23.3	D11S144	19	13	0.68	Cervix	PNAS 91:6953
22.3-23.3	D119144	15	3	0.2	Esophageal	CR:54:2996-
22.3-23.3	D11S144	17	5	0.29	Ovarv	BJC 67:268
22.3-23.3	D115144	4	2	0.5	Pancreas	CR 54:2761
22.3-23.3	D11S144	21	4	0.19	Sarcoma	CR 52:2419
22.3-23.3	D113144	4	0	0	Stomach	HG 89:445
23.3	D11529	47	15	0.32	Breast	CR 54:6270
23.3	D11929	1	0	0	Breast	CR 53:3804
23.3	D11S29	25	25	1	Cervix	BJC 71:814
23.3	D11529	. 2	1	0.5	Colon	GCC 6:45
23.3	D11S29	12	7	0.58	Melanoma	GCC 7:169
23.3	D11929	15	7	0.47	Ovary	BJC 67:268
23.3	D11S29	10	6	0.6	Stomach	CR 56:268
23	CD3	. 7	4.	0.57	Colon	- GCC 6:45
23.3	CD3	1	0	0	Lung	PN 91:5513
23.3	CD3	. 9	0	Ū	Lung	PN 91:5513
23.3	CD3	3	0	0	Lung	PN 91:5513
23.3	CD3	16	7	0.44	Ovary	BJC 67:268
23	CD3	4	2	0.5	Stomach	HG 89:445
23.3	CD3	36	-8	0.22	Stomach	CR 56:268
23	D11S528	42	16	0.38	Breast	CR 54:6270
23	D119528	44	7	0.16	Stomach	CR 56:268
22.3-23	THY1	33	14	0.42	Breast	CR 54:4591
22.3-23	THYL	6	<u> </u>	0.17	Stomach	HG 89:445
23.3-qter	D11S147	12	8	0.67	Ovary	BJC 67:268
22-23.3	APOC3	.35	12	0.34	Breast	CR 54:4586
22-23.3	APOC3	30	19	0.63	Cervix	PNAS 91:6953
22-23.3	APOC3	22	0	0	Pediatric Pediatric	HG 97:163
Unknown	D11S836	17	6	0.35	Ovary	Unknown
Unknown	D119934	. 30.,	5	0.17	Cervix	CR 56:197
23	ETS1	5	3	0.6	Colon	GCC 6:45
23	ET91	1	0	0	Lung	PN 91:5513
23	ETS1	4	0	0	Lung	PN 91:5513
23	ETS1	5	0	0	Lung	PN-91:5513
23	ETS1	1 22	0 3	0	Testis	CCG 52:72
Unknown	D118910	···········	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.14	<u>Head&Neck</u>	CR 54:4756
Unknown	D115910	31	0	0	Head&Neck	CR 54:4756
Uhknown	D119910	6	3	0.5	Kidney	GCC 12:76
Unknown	D11S910	30 33	5	0.17	Melanoma	CR 56:589
22.3-23	D115968		14	0.42	Breast	CR 54:4586
22.3-23	D11S968	25	14	0.56	Cervix	PNAS 91:6953
22.3-23	D119968	5	1	0.2	Kidney	PNAS 92:2954
22.3-23	D11S968	17	1	0.06	Kidney	PNAS 92:2854

Chromosome 11 - q Arm

22.3-23	D119968-	17	i	0.06	Kidnev	PNAS 92:2854
Unknown	Unknown	16	1	0.06	Brain	CR 50:5784
13	Unknown	25		0.04	Breast	
Unknown	D11S485	16	9	0.56	Cervix	JNC1 84:506
13	Unknown	7	Ó	0.30	77-77-70000000 TTCTT-1000000000000000000000000000000000	PNAS 91:6953
Unknown	D115129	7	1	0.14	Endocrine	N 328:524.
Unknown	D1191383	5	4	0.8	Endocrine	CR 51:1154
Unknown	D115460	7	3	0.43	Endocrine	CR 56:599
Unknown	D119476	2	1	0.43	Endocrine	GCC 12:73
Unknown	D115527	7	5	0.71	Endocrine	GCC 12:73
Unknown	D118546	4	0	0.71	Endocrine	CR 56:599
Unknown	D11S614	22	5	0.23	Endocrine Endocrine	GCC 12:73
Onknown	D119787	6	4	0.23		CR 56:599
Unknown	D115873	23	6	0.26	Endocrine	CR 56:599
Unknown	D115874	13	3	0.28	Endocrine	CR 56:599
Unknown	D11S490	19	9	0.47	Endocrine	CR 56:599
13	Unknown	7	Ö	0.47	Head&Neck	CR 54:1152
13	Unknown	10	0	0	Liver	BJC 67:1007
13-23	D11924	2	-0	o o	Liver	BJC 64:1083
14-22.3	D11S1240	53	12	0.23	Liver	JJ 81:108
13.1-13.4	D1181253	67	13	0.19	Lung	GCC 13:40
21-23.2	D11S1256	67	21	0.11	Lung	GCC 13:40
14-22.3	D11S1260	20	8	0.4	Lung	GCC 13:40
13.4-14	D11S1261	39	11	0.28	Lung	GCC 13:40
23.2-23.3	D1151263	65	11	0.17	Lung	GCC 13:40
23.2-23.3	D11S1265	50	14	0.28	Lung	GCC 13:40
14-22.3	D115126B	30	10	0.28	Lung	GCC 13:40
13-23	D11S24	2	0	0.33	Lung	GCC 13;40
24	D119488	17	5	0.29	Lung	PN 84:9252
Unknown	D11S85	15	5	0.23	Ovary	GQ 55:245
13	FOLRI	14	1	0.33	Ovary	CR 53:2393
13	Unknown	8	3	0.38	Ovary	BJC 67:268
Unknown	D1151818	38	11	0.38	Pancreas	BJC 65:809
13-23	D11524	2	0	0.29	Stomach	CR 56:268
13-23	D11924		n O	0	Stomach	CR 48:2988
Unknown	D115420	19	0	0	Uterus	CR_51:5632
NUE		2978	764	0.26	Uterus	CR 54:4294
			104	U.45		

Chromosome 12 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
12.1	-KRAS2	3	. 0	0	Uterus	CR 51:5632
Unknown	D12S16	16	1	0.06	Brain	CR 50:5784
Unknown	D12S16	12	2	0:17	Breast	CR 50:7184
Unknown	D12S16	23	2	0.09	Breast	CR 53:4356
Onknown	D1292	16	2	0.12	Cervix	CR 54-4481
Unknown	D12S87	24	2	0.08	Cervix	CR 56:197
Unknown	D12989	25	2	0.08	Cervix	CR 56:197
12.1	KRAS2	7	0	0	Colon	N 331:273
Unknown	D12S77	18	2	0.11	***	
Unknown	D12S16	26	1	0.04	Endocrine	CR 56:599
Unknown	D12516	7	2		Esophageal	CR 54:2996
Unknown	D12S62	28	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		Esophageal	GCC 10:177
Onknown	D12598	28 19	5	0.18	Head&Neck	CR 54:1152
Unknown				0.05	Head&Neck	
Unknown	D12S98	17	0	0	Head&Neck	CR 54:4756
****	D12916	10	. 0	0	Kidney	CR 51:820
	12S94-D12S77	5	1	0.2	Kidney	PNAS 92:2854
	012 594 -012577	20	0	0	Kidney	PNAS 92:2854
Unknown	D12S98	6	3	0.5	Kidney	GCC 12:76
Unknown	Unknown	43	. 8	0.19	Leukemia	B 86:3869
Unknown	Unknown	35	8	0.23	Leukemia	B 86:3869
Unknown	D12558	44	9	0.2	Leukemia	B 86:3869
Unknown	D12S64	54	7	0.13	Leukemia	B 86:3869
Unknown	D12969	4.6	4	0.09	Leukemia	B 86:3869
Unknown	D12589	82	21	0.26	Leukemia	B 87:3368
Onknown	D12689	. 50	11	0.22	Leukemia	B 86:3869
Unknown	D12S91	48	9	0.19	Leukemia	B 86:3869
Unknown [12594-D12577	51	6	0.12	Leukemia	B 86:3869
Unknown	D12S:89-91	50	13	0.26	Leukemia	CR 55:5377
Onknown	D12S16	12	1	0.08	Liver	CR 51:89
12.1	KRAS2	4	C	0	Liver	CCG 48:72
Unknown	DI2916	25	5	0.2	Lung	CR 52:2478
12.1	KRAS2	3	1	0.33	Lung	PN 84:9252
Unknown	D12598	19	Ô	0.33	PROPERTY OF THE PROPERTY OF TH	AND THE RESERVE OF THE PARTY OF
12.1	KRAS2	مر ند کاری 2	0	0	Melanoma	CR 56:589
	MASZ	4	U	U	Neuroblasto a	m CR 49:1095
13.3-12.3	A2M	10	1	0.1	Ovary	IJC 54:546
Unknown	D12516	8	3	0.38	Ovary	CR 51:5118
12-PTER	F8VWF	16	1	CONTRACTOR OF THE SECTION OF THE SEC	14.545.455. 231.55.555.5 5 .4444.494.494.494.49	
12.1	KRAS2	7	0	0.06	Ovary	BJC 69:429
Onknown	PRB1	23	2	******	Ovary	CR 50:2724
Unknown	D12S16			0.09	Ovary	CR 53;2393
12.1	THE PERSON NAMED AND POST OF PERSONS ASSESSED.	9	1	0.11	Prostate	G 11:530
12.1	KRAS2	4	1	0.25	Stomach	CR 48:2988
COMPANY CONTRACTOR CON	KRAS2	7	0	0	Testis	GCC 13:249
Onknown	PRB1-PRB4	11	2	0.18	Testin	LI 73:606
Unknown	D12S61	14	1	0.07	Uterus	CR 54:4294
12.1	KRAS2	33	0	O.	Uterus	CR 51:5632

WO 98/41648

PCT/US98/05419

100 / 214

Chromosome 12 - p Arm

SUM

959 141 0.15

Chromosome 12 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
Unknown	IGF1	11	1	0.09	Uterus	CR 54:4294
Unknown	Unknown	14	1	0.07	Brain	CR 50:5784
Unknown	D12S17	19	1,	0.05	Breast	CR 50:7184
14-24.1	D12S7	35	2	0.06	Breast	GCC 2:191
Unknown	D12917	8	1	0.12	Cervix	GCC 9:119
Unknown	D1257	31	1	0.03	Cervix	CR 54:4481
Unknown	D12578	31	6	0.19	Cervix	CR 56:197
Unknown	D12S83	22	1	0.05	Cervix	CR 56:197
Unknown	<u>D12917</u>	19,	1	0,05	Colon	CCG 48:167
Unknown	D12S17	17	4	0.24	Colon	IJC 53:382
14-24,1	D1297	22	3	0.14	Colon .	<u>N 331:273</u>
14-qter	D1258	24	4	0.17	Colon	N 331:273
24.3-gter	D12911	13	0	. 0	Endocrine	N 328:524
Unknown	D12S392	16	1	0.06	Endocrine	CR 56:599
Unknown	D12S43	23	0	0	Endocrine	GCC_13:9
Unknown	D12S14	18	3	0.17	Esophageal	CR 54:2996
Unknown	D12917	9	1	0:11	Esophageal	AND AND AND AND AND AND AND AND AND AND
Unknown	D12S17	34	3	0.09	Esophageal	GCC 10:177
Unknown	D12S17	23	2	0.09	Esophageal	CR 54:2996
Unknown	D12S60	24	6	0.25	Head&Neck	CR 54:1152
Unknown Unknown	D12986 D12586	24	4	0.17	Head&Neck	CR 54:4756
Unknown	D12586	18 24	0 0	0	Head&Neck	CR 54:4756
Unknown	D12517	6	3	0.5	Kidney Kidney	CR 51:820 GCC 12:76
Unknown	D12997-D12986	19	0	0.3	Kidney	PNAS 92:2854
Unknown	D12S97-D12S86		0	0	Kidney	PNAS 92:2854
24.3-gter	Unknown	12	i	0.08	Liver	BJC 64:1083
24.3-gter	Unknown	7	0	0	Liver	BJC 67:1007
Unknown	D12917	14	1	0.07	Liver	CR 51:89
Unknown	D12S17	15	1	0.07	Liver	JJCR 81:108
Unknown	D12S17	29	4	0.14	Lung	CR 52:2478
Unknown	D12586	23	0	0	Melanoma	CR 56:589
Unknown	D12917	25	- 5	0,24	Ovary	CR 53:2393
Unknown	D12S17	15	5	0.33	Ovary	CR 51:5118
Unknown	D12560	15	2	0.13	Ovary	BJC 69:429
22-24.2	PAH	26	2	0.08	Ovary	IJC 54:546
24:3-gter	Unknown	13	Ō	0	Pancreas	BJC 65:809
24.3-gter	Unknown	6	3	0.5	Pancreas	CR 54:2761
Unknown	D12S17	6	ο	0	Pancreas	CR 54:2761
14-24.1	D12S7	17	1	0.06	Prostate	G 11:530
Unknown	D12917	26	Š	0.19	Sarcoma	CR 52:2419
CEN-q14	D1254	5	1	0.2	Sarcoma	CR 52:2419
2.4-ter	Unknown	11	. 6	0.55	Stomach	BJC, 59;750
24.3-qter	D12S11	32	5	0.16	Stomach	HG 92:244
Unknown	D12S17	41	11	0.27	Stomach	CR 51;2926.
12-13.2	COL2A1	11	0	0	Testis	GCC 13:249

Chromosome 12 - q Arm

SUM		1096	147	0.13		
Unknown	IGE1	11	1	0.09	Oterus	CR 54:4294
Unknown	D12S60	17	1	0.06	Uterus	CR 54:4294
Unknown	D12917	23	4	0.17-	Urerus	GCC 9:119
14-qter	D12S8	8	1	0.12	Testis	0 9:2245
Onknown	D1297	19	8	0.42	Testis	0.9:2245
Unknown	D12S7	1	0	0	Testis	CCG 52:72
Unknown	D1257	3	0	0	Testis	CCG 52:72
Unknown	D12S7	1	0	0	Testis	CCG 52:72
14-24.1	D1297	: 15	Q	.0	Testis	GCC 13:249
14-24.1	D12S7	6	1	0.17	Testis	LI 73:606
Jnknown	D12S6	17	7	0.41	Testis	0 9:2245
CEN-al4	D12S4	23	4	0.17	Testis	0 9:2245
Jaknowa	D12517	26	7	0.27	Testis	0.9:2245
Jnknown	D12S15	14	1	0.07	Testis	0 9:2245
Jaknowa	D12914	19	3	0.16	Testis	0 9:2245
Jnknown	D12S12	15	7	0.47	Testis	0 9:2245
4.3-qter	D12511	30	0	G	Testis	GCC 13:249

Chromosome 13 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
12	D13536	19	5	0.26	Ovary	TJC 54:546
12	D13S36	19	3	0.16	Ovary	IJC 52:575
12.3	D13911	9	3	0:33	Ovary	IJC 54:546
12.3	D13S11	6	5	0.83	Sarcoma	CGC 53:45
Unknown	D13S115	13	6	0.46	HeadaNeck	CR 54:1152
Unknown	D13S115	16	2	0.12	Ovarv	BJC 69:429
Unknown	D135721	28	7	0.25	Bladder	Unknown
Unknown	D13S221	39	17	0.44	Breast	GCC 13:291
12.3	D1396	-4	2	0.5	Breast	PNAS 8412372
12.3	D13S6	13	5	0.38	Colon	IJC 53:382
12.3	D13S6	1	0	0	Colon	CCG 48:167
12.3	D13S6	8	2	0.25	Ovary	IJC 54:546
,12.3	D1396	9	0	0	Stomach	G 2:180#-2-
12.3	D13S6	7	2	0.29	Uterus	CR 51:5632
Unknown	D135289 **	35	17	0:49	Breast	GCC 13:291
12	FLT1	7	C	0	Brain	CR 54:1397
12	FLT1	9	3	0.33	Brain	CR:54:1397
12	FLT1	18	6	0.33	Ovarv	CR 54:605
12	FLT1	5	1	0.2	Ovary	BJC 69:429
12.3	D13533	21	4	0.19	Ovary	IJC 54:546
12.3	D13S33	23	6	0.26	Ovary	IJC 52:575
12	D13S260	43	13	0.3	Breast	GCC 13:291
13	D1381	94	26	0.28	Bladder	0.6;2305
14-12	D13S1	34	7	0.21	Breast	GE 5:554
13	D1351	8	3	0.38	Breast	PNAS 84:2372
13	D13S1	13	4	0.31	Breast	GCC 2:191
13	D1351	7	7	0.29	Cervix	CR 49:3598
14-12	D13S1	11	1	0.09	Colon	JNCI 84:1100
13	D1351	15	7	THE PROPERTY OF STREET AND VALUE OF	CONTRACTOR OF THE COLOR NOTIONS AND THE	
12	D13S1	12	******************************	0.47	Colon	IJC 53:382
13	D1351	14	1 4	0.08	Colon	CCG 48:167
13	D1351	10	**************************************	0.29	Esophageal	CR 54:2996
13	D1351	25	2 5	0.2	Kidney	CR 51:1071
14-12	D1351	15		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Liver	JJCR 84:893
14-12	D1351	. 5	5 .2	0.33 0.4	Liver	CR 54:281
12	D1351	9	***************************************		Liver	
14-12	D1351	9	0	0	Liver	JJCR 81:108
13	and the same and t			0,67	Liver	CR 51:4367
14-12	D13S1	19	8 7	0.42	Lung	PN 84:9252
	D13S1	8	******************************	0.88	Lung	CR 49;5130
12	D13S1	1	0	0	Lung	PN 84:9252
.13	D13S1	5,	0	0	\$7\$C0\$ \$2000000000000000000000000000000000	m CR 49:1095
13	D13S1	15	2	A 12	a	IJC 54:546
13	D1351 D1351	15 12	2 9	0.13	Ovary	CR 52:2419
13	D1351			<u>, 6,75</u>	Sarcona	***************************************
14-12	C. CO. Province Constitution of Constitution o	6 10	0	0	Stomach	HG 89:445
19714	01351		1	1,0	Stomach	CR 48:2988

Chromosome 13 - q Arm

14-12	D13S1	11	1	0.09	Testis	LI 73:606
13	01351	3	0	0	Testis	CCG 52172/y
13	D13S1	3	1	0.33	Testis	CCG 52:72
13	D13S1	1	0	0	Testis	CCG 52:72 ⁻⁷⁰
13	D13S1	8	1	0.12	Uterus	CR 51:5632
12	D13S267	32	16	0.5	Breast	GCC 13:291/
14	D13S218	140	33	0.24	Leukemia	CR 55:2044
12	D13S263	45	20	0.44	Breast	GCC 13:291
14	D13S22	17	5	0.29	Breast	GE 5:554
14	D13822	11	3	0.27	Breast	GE 15:55425
14	D13S22	12	0	0	Pediatric	CR 50:3279
14	013822	- 8	7	0.88	Sarcoma	CGC 53:45/A
14	D13S153	42	15	0.36	Breast	GCC 13:291
14.3	D13S133	16	10	0,56	Head&Neck	CR 54:1152.
14.3	D13S133	6	3	0.5	Kidney	GCC 12:76
1473	D13S133	140	5	0.04	Leokemia	CR 55; 2044
14.3	D13S133	11	0	0	Ovary	CR 54:605
14.3	D138133	18	11	0.61	Ovary	CR 54:605
14.3	D13S133	21	7	0.33	Prostate	HUPATH 27:28
14.3-21.1	D13531	29	9	0.31	Ovary	IJC 52;575
14.3-21	D13531	26	6	0.23	Ovary	IJC 54:546
14	RB	94	28	0.3	Bladder	0 6:2305
14	RB	9	4	0.44	Brain	0 6:445
10	RB	20	3	0.15	Breast	AJP 140:215
14	. RB	38	6	0.16	Breast	CR 53:4356
14.1	RB	14	5	0.36	Breast	JNCI 84:506
14	RB	10	4	0.4	Breast	GCC 4:113
19	RB	32	12	0.38	Ereast	GE 5:554
14 14	RB	37	12	0.32	Breast	GCC 4:113
	P.B	90	23	0.26	Breast	CR 52:2991
14 14	RB	14	0	C	Cervix	BJC 67:71
	R.B	27	9	0.33	Colon	CR 52:741
14.1	RB	25	12	0.48	Colon	IJC 53:382
14.1	RB	156	18	0.12	Colon	BJC 64:475
19	RB	39	10 Q	0.26	Colon	GAST 104:163
14	88		***************************************	0	Colon	JNCI 84:1100
14	RB RB	6	0 0	C O	Colon	JNCI 84:1100
14	RB	42 29			Endocrine	C 74:693
10	Contraction of the Contraction o	4D	17 19	0.59	Esophageal	C 73:2472
14	RB RB	8 8	4-22-27-27-27-2-24-24-42-42-44-44-44-44-44-44-44-44-4	0.47	Esophageal	CR 51:5766
14	SSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS	16	1 .5	0.12	Esophageal	CR 51:2113
14	RB RB	1.6 50		0,31	Esophageal	CR 54:29961
14	RB RE	50 29	24 17	0.48	Esophageal	CR 52:6525
14	RB	11			<u>Head&Neck</u> Liver	CR 54:281
14	RB	11	4 3	0.36 0.27	Liver	CR 51:4367
Uli A.Z.		***		U. Z.	PTAGE	CK 371.4301

WO 98/41648 PCT/US98/05419

Chromosome 13 - q Arm

14	RB	9	1	0.11	Liver	CR 51:4367
14	P.B	67	13	0.19	Lung	0 8:1913
14	RB	16	0	0	Lung	0 9:39
14	RE	7	2	0.29	Lung	CR 54:5643
14	RB	20	12	0.6	Lung	0 8:1913
14	RB	8	0	0	Lung	5 241 353
14	RB	3	2	0.67	Lung	CL 71:67
14	RE	8	6	0.75	Lung	0 9:39
14	RB	76	28	0.37	Lung	0 8:1913
14	RB	27	14	0.52	Lung	CR 54-56435
14	RB	59	22	0.37	Lung	0 10:937
14	RB	5	4	0.8	Lung	CR 54:56434
14	RB	2	1	0.5	Lung	CL 71:67
14	PB	7	-	0.14	Ovary	GO 55:245
14	RB	13	8	0.62	Ovary	IJC 58:663
16	R.B	31	23	0.74	Overy	CR 54:610
14	RB	39	13	0.33	Ovary	IJC 54:546
14.1	RB	17	2	0.12	Ovary	CR 54:610%
14	RB	33	9	0.27	Ovarv	IJC 52:575
10	RB	-4B	25	0.52	Ovary	CR 54:610
14	RB	9	0	0	Pediatric	CR 50:3279
14	R.B	13	3	0.23	Prostate	PNAS 87:8751
14.1	RB	9	6	0.67	Prostate	BJU 73:390
14	RB	19	7	0.37	Prostate	BUPATH 27:28
14	RB	40	24	0.6	Prostate	BJC 70:1252
14	RB	7	5	0.71	Sarcoma	CR 52:2419
14	RB	13	4	0.31	Stomach	LI 74:835
14	R.B	31	12	-0.39	Testis	0 9:2245
Unknown	D13S155	6		0.5	Kidnev	GCC 12:76
Unknown	D13S155	32	3	0.09	Melanoma	CR 56:589
14.1	D13S118	21	7	0.33	Prostate	HUPATH 27:28
21.1-21.2	D13526	27	17	0.63	Overy	GO 47:137
21-qter	D13S12	7	1	0.14	Liver	PNAS 86:8852
21-qter	D13512	4	q	1	Sarcoma	CGC 53:45
22	D13S2	94	26	0.28	Bladder	0 6:2305
Dnknown	D1352	6	1	0.17	Breast	GCC 2:191
22	D13S2	7	3	0.43	Breast	PNAS 84:2372
22	D1352	2	0	0.43	Cervix	CR 49:3598
22	D13S2	4	1	0.25	Cervix	CR 54:4481
22	D1352	10	3	0.3	characteristrate recovers a substitution	1JC 53:382
22	D1352	8 Tu	0	0.3	Colon Colon	CCG 48:167
22	***************************************	8 4	<u>i</u>	0.25	*****	CCG 48:167
	D13S2			a natural parts of a relative PM - Mrs bridge on a capacitage as	Colon	CCG 48:187 CR 54:2996
22	D13S2 D13S2	17 6	7 2	0.41 0.33	Esophageal	CR 51:1071
22	Charles and development of the same of the property of the	APPROXIMATION	ACTIVITY OF THE PROPERTY OF THE PARTY OF THE	AND AND AND AND AND AND AND AND AND AND	<u>Kraney</u>	CCG 48:72
22 22	D1352	6	4	0.67	Liver	CCG 48:72 CR:51:89**
22,	<u>D1382</u>	13		0.23	Liver	

Chromosome 13 - q Arm

Unknown	D13S2	13	0	0	Liver	JJCR 81:108
22	01352	21	12	0.57	Lung	PN 84:9252
22	D13S2	12	2	0.17	Lung	JJCR 80:924
Unknown	D1392	9	7	0.78	Lung	CR 49:5130
22	D1352	7	1	0.14	Neuroblaston	CR 49:1095
Unknown	D1352	10	3	0.3	Ovary	IJC:54:546
22	D13S2	8	6	0.75	Sarcoma	CR 52:2419
22	D13S2	10	4	0.3	Stomach	CR 52:3099
22	D1352	9	1	0.11	Stomach	HG 92:244
22	D1332	11	2	0.18	Stomach	CR 48:2988
22	D13S2	6	4	0.67	Stomach	G 2:180
Unknown	D1382	7	1	0.14	Stomach	HG 89:445
Unknown	D1352	14	4	0.29	Testis	0 9:2245
22	D1352	4	4	0.25	Oterus	CR 51:5632
	D13S170	47		0.23		GCC 13:291
22-31	·····	29	11	0.23	Breast	CR 54(4756
22-31	D13S170				Head&Neck	A STATE OF A STATE OF
22-31	D13S170	20	0	0	Head&Neck	CR 54:4756
31	D1354	<u> </u>	1	1	Breast	GCC 2:191
Unknown	D13S4	26	3	0.12	Breast	GE 5:554
Unknown	01354	5	2	0.4	Breast	PNAS 84:2372
Unknown	D13S4	10	0	0	Cervix	CR 49:3598
31	D1354	8	0	0	Colon	JNCI 84:1100
Unknown	D1354	1	0	0	Colon	CCG 48:167
Unknown	D1354	19	12	0.63	Colon	IJC 53:382
Unknown	D13S4	12	4	0.33	Esophageal	CR 54:2996
Unknown	D1354	. 4	0	0	Traex.	JJCR 81:108
31	D1354	19	10	0.53	Lung	PN 84:9252
31	D1354	16	3	0,19	Lung	JJCR 80:924
Unknown	D13S4	5	5	1	Lung	CR 49:5130
31	D1354	8	0.	.0	Neproblasto a	m CR 49:1095
Unknown	D1354	15	11	0.73	Sarcoma	CR 52:2419
31	D1354	14	3	0.21	Stomach	RG 92:244
Unknown	D13S4	11	2	0.18	Stomach	G 2:180
Unknown	D1384	17	2	0.12	Stomach	CR 48:2988
Unknown	D1354	12	0	0	Uterus	CR 51:5632
22-34	D13S5	26	6	0.23	Breast	GE 5:554
21.3-32	D13S5	4	1	0.25	Breast	PNAS 84:2372
21.3-32	D1355	15	4	0.27	Colan	TJC 53:382
21.3-32	D13S5	4	0	0	Colon	CCG 48:167
22-34	D1385	1	0	0	Colon	JNCI 84:1100
22-34	D13S5	22	9	0.41	Ovarv	IJC 54:546
21.3-32	D1355	10	4	0.4	Stomach	G 2:180
22-34	D13S5	7	1	0.14	Stomach	G 2:180
21.3-32	D1335		Ċ	0.14	Oterus	CR 51:5632
22-34	D13S5	3	0	0	Uterus	CR 51:5632
22-34	2222	د	J	U		

PCT/US98/05419

Chromosome 13 - q Arm

21	D13971	15.	2	0.13	Brain "	CR 54:1397
21	D13S71	7	0	0	Brain	CR 54:1397
32-34	D13S128	34	. 12	0,35	Owary	CR 54:605
34	D13534	12	5	0.42	Ovary	IJC 52:575
34	D13934	15	7	0.47	Ovary	IJC 54:546
34	D13S32	28	11	0.39	Ovary	IJC 54:546
34	013832	26	12	0,46	Ovary	IJC 52:575
22-31	D13S173	39	7	0.18	Breast	GCC 13:291
34	D1383/	94	26	0.28	Bladder	0.6:2305
Unknown	D13S3	20	3	0.15	Breast	GCC 2:191
34	D1393-	2.5	. 4	0.15	Breast	GE 5:554
34	D13S3	7	2	. 0.29	Breast	PNAS 84:2372
33-34	D1353 :	27	- 3	0.11	Cervix	CR 54:4481
34	D13S3	18	4	0.22	Cervix	CR 49:3598
	D1393	15	6		Colon	IJC 53:382
Unknown	D13S3	6 • 4	0 Q	0	Colon	JNCI 84:1100
Unknown	D1383	*********			Liver	JJCR 81;108;
33-34 34	D13S3	2	1	0.5	Liver	CCG 48:72
34	D1393	B	4	0.5	Liver	CR 51:4367
Unknown.	D13S3	23	4	0.44	Lung	PNAS 86:5099 PN 84:9252
34	D1353 D1353	23 11	10	0.3 0.91	Lung Lung	CR 49:5130
34	D1353	24	9	0.38	Lung	PN 84:9252
34	D1353	9	4	0.44	Lung	PNAS 86:5099
34	D1353	7	1	0.14	Neuroblast	
	21.303		-		ä.	COR CR 1314030
34	D13S3	21	3	0.14	Ovary	IJC 52:575
34	D1383	19	4	0.21	Ovary	IUC 54:546
Unknown	D13S3	9	4	. 0.44	Sarcoma	CR 52:2419
34	D1393	5	0	Ö	Stomach	HG 89:445
34	D1353	20	5	0.25	Stomach	G 2:180 '
33-34	D1383	9	1	0.11	Stomach	RG 92;244
Unknown	D13S3	19	5	0.26	Stomach	G 2:180
33-34	D1393	17	22	0.12	Stomach	CR 48:2988
Unknown	D13S3	1	0	Ô	Testis	CCG 52:72
34	01363	20	8	0.4	Testis	0.9:2245
Unknown	D13S3	4	0	0	Testis	CCG 52:72
Unknown	D1393		9.3	0	<u>Testis</u>	CCG 52:72
34 34	D1353	7 17	1 2	0.14	Uterus	CR 51:5632
34	D13935			0.12	Ovary	IJC 54:546
22000000000000000000000000000000000000	D13535	18 33	2 7.	0.11	Ovary	CR 50:7184
Unknown Unknown	D13S52		*****	0.21	Breast	CR 51:5794
Unknown	D13S52	132 - 53	34 23	0.26	Breast	CONTRACTOR OF THE PROPERTY OF
Unknown	D13552	16	***************************************	0.19	Esophagea Esophagea	
Unknown	D13552	22	3 10 :	THE RESERVE AND A SHARP OF THE PARTY OF THE	Esophagea Esophagea	
Unknown	D13552	20	3	0,45 0.15	Kidney	CR 51:820
Ulikilowii	D12225	20	3	0.15	vramel	CK 31.020

PCT/US98/05419 WO 98/41648 108 / 214

Chromosome 13 - q Arm

Unknown	D13952	26	4	0.15	Liver	CR 51:89
Unknown	D13S52	2	1	0.5	Lung	CR 52:2478
Unknown	013552	9	5	0.56	Lung	CR 52:2478
Unknown	D13S52	26	5	0.19	Lung	CR 52:2478
Unknowa	D13952	1	1	1	Lung	CR 52:2478.*
Unknown	D13S52	27	6	0.22	Ovary	CR 51:5118
34	F 7	11	2	0.18	Ovary	IJC 54:546
34	E 7	11	2	0.18	Ovary	IJC 54:546
Unknown	BRAC2 (D135:263-	1	-1	1	Bladder .	CR 55048301
	219-220-267-171-					
	260-2171	3	0	0	Bladder	CR 51:5405
Unknown	D13S30	30			Bladder	CR 55:5213/
Unknown	D139:133-170	•		0.14	Brain	CR 49:6572
Unknown	Unknown	7	1 2		Brain	CR 50.5784
Unknown	<u>Onknown</u>	14 13	2	0.15	Brain	CR 54:1397
32	D13S193	13	2	• 0	Brain	CR:54:13976
32	D13S193	7	0	0	Brain	CGC 73:122
Unknown	RB1-D13S4-D13S63	1.8	2	0.11	Brain	CGC 73:122
Unknown	RB1-D13S4-D13S63	10	0	0.22	Brain	CGC 73:122
Unknown	RB1-D13S4-D13S63	10	-1	1	Breast	CR 55:4830
Unknown	BRAC2 [D135:263- 219-220-267-171-	± , "	-1	-	Drease	CN 20.7000
	260-2171					
Unknown	BRAC2 (D135:263-	33	28	0.85	Breast	CR 55:4830
	219-220-267-171-					
	260-217)					Din C 04-2272
Unknown	D13S7	2	1	0.5	Breast	PNAS 84:2372 CR 55:4830
Unknown	BRAC2 (D13S:263- 219-220-267-171-	1	1	1	Cervix	CK 55:4650
	260-217)					
Unknown		6	٥	0	Colon	JNCI 84:1100
Unknown	BRAC2 (D135:263-	1	1	1	Colon	CR 55:4830
	219-220-267-171-	-	_			
	260-217)	****				
Unknown	D13S10	5	0		Colon	CCG 48:167
Unknown	D13S37	21	1	0.05	Colon	CCG 48:167
Unknown	ESD	19	0	0	<u>Colon</u>	CCG '48:167
Unknown	D13S168	18	2	0.11	Endocrine	CR 56:599 PNAS 92:2854
Dakaowa	D135174-D135173	20	1	0.05	Kidney	
Unknown	D13S174-D13S173	5	0	0	Kidney	PNAS 92:2854
.Unknown	D135:156-158-164-	24	3	0.12	Leukemia	CR 55:5377
	217-221		^	^	Liver	BJC 64:1083
Unknown	Unknown	11	0	0	Liver	BJC 67:1007
Unknown	Unknown	5	0	0	Liver	BJC 67:1007
Unknown	14.2	****	1	•	Liver	PNAS 86:8852
pll-qll	D13S11	1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0,75	Lung	CR 54:2322
Unknown	Unknown	24	19 1:	CONTRACTOR CONTRACTOR	Lung	PN 86:5099
33-qter	Amada	3	A CONTRACTOR OF THE PROPERTY OF THE PARTY OF	0.33	Lung	PN 86:5099
33-ater	Unknown	9	4	0.44	Lung	FR 00.3033

Chromosome 13 - q Arm

33-qter	Unknown	9	4	0.44	Lung	PN 86:5099
Unknown	BRAC2 (D13S:263- 219-220-267-171- 260-217)	6	5	0.83	Ovary	CR 55:4830
Unknown	D13\$3-2-1-RE1	32	18	0.56	Ovary	CR 53:2353%
Unknown	Unknown	7	0	0	Pancreas	BJC 65:809
Unknown	14.2	10	0	Ö	Pancreas	BJC 65:809
Unknown	Unknown	13	3	0.23	Prostate	CSurveys 11:
Unknown	BRAC2 [D135:263- 219-220-267-171- 260-217]	7	6	0.86	Prostate	CR 55:4830
Unknown	D13S3-D13S5	11	1	0.09	Prostate	G 11:530
Unknown	D135103	32	5	0.16	Stomach	RG 92:244:
Unknown	D13S409	14	2	0.14	Stomach	CR 55:1933
Unknown	Unknown	15	3	0.2	Testis	G 5:134
Unknown	D13S103	9	1	0.11	Testis	GCC 13:249
Unknown	D13970	13	3	0.23	Testis	GCC 13:249
Unknown	D13S120	15	0	00	Uterus	CR 54:4294
Unknown	D13S122	18	2	0.11	Uterus	CR 54:4294
SUM		5208	1509	0.29		

110 / 214

Band	Marker Total	Cases wi/LOH	LOH Freq.	Tumor Type	Reference
SUM	D14522 24 24	2 2	0.08	Esophageal	CR 54:2996

WO 98/41648 PCT/US98/05419

Chromosome 14 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freg.		
Unknown	TCRD	31	6	The state of the s	Tumor Type	Reference
Unknown	D14S:267-268-51	30	21	0.19	Uterus	CR 54:4294
Unknown	Unknown	19	3	0.7	Bladder	CR 55:5213
32	D14513	14	1	0.16	Brain	CR 50:5784
32.1-32.2	D14913	2 6	1	0.07	Brain	CR 49:6572
32.1-32.2	D14S13	26	1	0_04	Brain	CR 55:4696
32	D14S16	26	1	0.04	Brain	CR 55:4696
32	D14S16	26	1	0.04	Brain	CR 55:4696
32.3233	D14523	26	0	0.04	Brain	CR 55:4696
32.3233	D14S23	26	0	<u> </u>	Brain	CR 55:4696
24.3	D14S43	26	5	0	Brain	CR 55:4696
24.3	D14S43	26	5	0.19	Brain	CR 55:4696
32,1-32.2	D14845	26	. 1	0.19	Brain	CR 55:4696
32.1-32.2	D14S45	26	1	0.04	Brain	CR 55:4696
24.3-31	D14948	26	8		Brain	CR 55:4696
24.3-31	D14S48	26	8	0.31	Brain	CR 55:4696
32.1-32.2	D14S51	26	3	0.31	Brain	CR 55:4696
32.1-32.2	D14S51	26	3	0,12	Brain	CR 55:4696
12.0-13.0	D14S54	26	2	0.12 0.08	Brain	CR 55:4696
12.0-13.0	D14S54	26	2		Brain	CR 55:4696
23-31	D14859	26	10	0.08	Brain	CR 55:4696
23-31	D14S59	26	10	0.38	Brain	CR 55:4696
12.0-13.0	D14S70	26	8	0.38 0.31	Brain	CR 55:4696
12.0-13.0	D14570	26	9	0.31	Brain	CR 55:4696
24.3-31	D14976	26	6	0.31	Brain	CR 55:4696
24.3-31	D14S76	26	6	0.23	Brain	CR 55:4696
12	D14580	26	7	0.27	Brain	CR 55:4696
12	D14580	26	7	0.27	Brain Brain	CR 55:4696
31	D14981	26	7	0.27	Brain	CR 55:4696
31	D14S81	26	7	0.27	Brain	CR 55:4696
32.3	IGH	26	9	0.35	Brain	CR 55:4696
32.3	IGH	26	9	0.35	Brain	CR 55:4696
32	D14913	60	7	0.12	Breast	CR 55:4696
32	D14S13	29	7	0.24	Breast	CR 53:4356 GCC 2:191
32	D14S13	4.7	6	0.13	Breast	CR 50:7184
32	D14516	17	2	0.12	Breast	GCC 2:191
32.3	IGH	6	. 2	0,33	Breast	CR 53:3804
32.3233	D14S1	10	2	0.2	Cervix	CR 49:3598
32.33	D14S20	10	1	0.1	Cervix	CR 54:4481
Unknown	D1453	7	0	0	Cervix	GCC 9:119
32.1	AACT	26	6	0.23	Colon	0 8:671
32.32-32.33	AKTI	10	4	0.4	Colon	0 8:671
32,32-,33	D14S1	42	14	0.33	Colon	0 8:671
32.33	D14S1	28	12	0.43	Colon	IJC 53:382
32	D14913	35	14	0.4	Colon	IUC 53:382
Unknown	D14S16	17	2	0.12	Colon	CCG 48:167

Chromosome 14 - q Arm

32	D14S16					
32	D14S16			0.5	Colon	IJC 53:382
32.3233		37 12	18	0.49	Colon	0 8:671
32.3233	D14517		- 5	0.42	Colon	IJC 53:382
32.1-32.32	D14517	20	7	0.35	Colon	0 8:671
32.32-32.33	D14S19	1	- 1	1	Colon	IUC 53:382
32.33	D14519	39	22	0.56	Colon	0 8:671
32.33	D14S20	14 20	4	0.29	· Colon	IJC 53:382
32.1-32.32	D14521	20	10	0.5	Colon	0 8:671
32.1-32.32	D14521	23	2		_^ Color	IJC, 53:382
32.3233	D14523	23	6 9	0.26	Colon	0 8:671
32.3233	D14S23	42	***************************************	0,39	Colon	IUC 53:382
32.3	IGH	47	21	0.5	Colon	0 8:671
32.1	PI	6	26	0.55	Colon	0.8:61
Ugknown	D14S174	21	0	0	Colon	0 8:671
32.1-32.2	D14S45	23	0	0	Endocrine .	GCC 13:9
32	D14S13	23	4	0	Endocrine	CR 56:599
32	D14S13	64	9	0.17	Esophageal	CR:51:2113
32	D14513	26	4	0.14	Esophageal	GCC 10:177
Unknown	D14S51	23	9	0.15	Esophageal	CR 54:2996
Unknown	D14573	20	1	0.39	Head&Neck	CR 54:1152
Unknown	D14S73	18	1	0.05	Read&Neck	CR 54:4756
-32	D14513	36	3	0.06	Head&Neck	CR 54:4756
Unknown	D14S65-D14S81	6	1	0.08	Kidney	CR 51:820
Unknown	D14S65-D14S81	22	5	0.17	Kidney	PNAS 92:28
Unknown	Unknown	10	0	0.23	Kidney	PNAS 92:28
Unknown	Unknown	5	Ö	0	Liver	BJC 64:108
32.3233	D14S1	3	0	0	Liver	BJC_67:100
32.3233	D1451	17	6	0.35	Liver	CCG 48:72
32	D14S13	46	5	0.33	Liver	JJCR 81:10
Unknown	D14815	2	0	0.11	Liver	CR 51:89
32.3233	D14S1	1	1	1	Liver Luna	PNAS 86188
32.32-,33	D1451	17	7	0.41		CR 54:5643
32.3233	D14S1	8	1	0.12	Lung Lung	CR 54:5643
32,3233	D14S1	23	2	0.09	Lung	CR 54:5643
32	D14S13	50	6	0.12	Lung	PN 84:9252
32.33	D1451	22	7	0.32	Neurchlastor	CR 52:2478
32.3233					a	. 0 /:1165
32.3233	D14S1	16	8	0.5	Neuroblaston	CR 49:1095
32:3233					a	
	D14S1_	19	4	0.21	Neuroblaston	ı 0 7:1185
32.1-32.2	D14S13	24	-	-	_a	
		44	5	0.21	Neuroblaston	0 7:1185
32	D14S15	13	8	0.62	a	
			•	U. DZ.	Neuroblaston	0.7:1185
32.3233	D14S17	18	1	0.06	Neuroblaston	0.7.1105
					a	

Chromosome 14 - q Arm

32.32-32.33						
32.32=32.33	D14S19	20	4.	-0.2	Neuroblast	om: 0 7:1185
32.1-32.32	D14S21	18	1	0.06	Neuroblass	om 0 7:1185
11.2-13			***************************************		a	om 0 7:1185
14.2.10	AHYM.	17	0	0	Neuroblast	om 0 7:1185
32.3233	D14S1	26	2		. a	
32	D14913	28'		0.08	Ovary	IJC 54:546
32	D14516	15	5	0.18	Ovary	CR 51:5118
32.33	D14S20	9	7	0.47	Ovary	CR 53:2393
Unknown	D14S34	13	3	EE.0	Ovary	0.7:1059
24.3-31	D14548	13	7	0.54	Ovary	BJC 69:429
Unknown	D14S49	20	3	0.33	Ovary	BJC 69:429
Unknown	D14S50	10	5	0.25	Ovary	BJC 69:429
Unknown	D14S51	17	3	0.3	Ovary	BJC 69:429
Unknown	Unknown		4	0.24	Ovary	BJC 69:429
32	D14S13	6	0	0	Pancreas	BJC 65:809
32,32-,33	D1451	4	0	0	Pancreas	CR 54:2761
32.3233	D14S1		0	0 1	Prostate	G 11:530
32	D14813	7	0	0	Sarcoma	CR 52:2419
32.3233	D14513	29	11	0.03	Sarcoma	CR 52:2419
Unknown	TO STATE OF THE PARTY OF THE PA	16	1	0.06	Stomach	CR 48:2986
32.33	D14544	32	5	0.16	Stomach	HG 92:244
Unknown	D14S20	8	1	0.12	Testis	0 9:2245
32.3233	D14844	21	2	0.1	Testis	GCC 13:249
Unknown	D14S1	10	0	C	Uterus	CR 51:5632
24.3-31	D1453	12	1	0.08	Uterus	GCC 9:119
II.2-13	D14S76	28	3	0.11	Uterus	CR 54:4294
Unknown	МУН6	18	2	0.11	Uterus	CR 54:4294
The state of the s	TCRD	31	6	0.19	Uterus	CR 54:4294
SUM		2442	542	0.22		CAN 34.4294
				***************************************		***************************************

Chromosome 15 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freg.	Tues - Tues	
Unknown	D15S25	26		0.15	Tumor Type	Reference
Unknown	D15S25	9	0	ρ	Colon	CR. 54:2996
Unknown	D15S25	26	4	0.15	reash1	CCG 48:167
SUM		35	4	0.11	ssopnageat	CR:54:2996

Chromosome 15 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
26.1	FES	36	5	0.14	Uterus	CR 54:4294
Unknown	Unknown	18	3	0.17	Brain	CR 50:5784
Unknown	D15S27	7	1	CONTROL OF THE PARTY OF THE PAR	Brain	CR 49: 6572
14-21	D15S1	28	1	0.04	Breast	GCC 2:191
11-12.0	015511	34	3	0.09	Breast	CR 53:4356
pter-ql3	D15S24	2	1	0.5	Breast	CR 53:3804
Unknown	D15S28	12	2	0.17	Breast	CR 50:7186
Unknown	D15S29	16	4	0.25	Breast	GCC 2:191
14-21	D15S1	- 6	0	0	Cervix	CR 49.3598
pter-q13	D15S24	23	0	0	Cervix	CR 54:4481
14-21	D15S1	6		0.17	Colon	N 331:273
Unknown	ACTC	36	6	0.17	Endocrine	CR 56:599
Unknown	CYP19	33		0.15	Endocrine	****
14-21	D15S1	5	4	0.8	Endocrine	CR 56:599
Unknown	D159100	31	5	0:16	Endocrine	***************************************
Unknown	D15S107	8	6	0.75	Endocrine	CR 56:599
Unknown	D15S108	- 8	3	0.38	Endocrine	****
Unknown	D15S114	4	4	1	Endocrine	CR 56:599
Unknown	0159116	21	7	0.33	Control of the contro	CR 56:599
Unknown	D15S118	16	5	0.31	Endocrine	CR 56:599
Unknown	D15S125	24	5	0.21	Endocrine	CR 56:599
Unknown	D15S127	10	7	0.7	_Endocrine	CR 56:599
Unknown	D15S144	9	7	0.78	Endocrine	CR 56:599
Unknown	D15S165	32	7	0.22	Endocrine	CR 56:599
Unknown	D15587	20	7	0.35	Endocrine	CR 56:599
Unknown	D15S97	32	8	0.25	Endocrine	CR 56:599
Unknown	GABR83	31	7	STATE OF COMMENTS	Endocrine	CR 56:599
Unknown	D15S27	17	2	0.23 0.12	Endocrine	CR 56:599
Unknown	015827	27	2	0.12	Esophageal	GCC 10:177
Unknown	D15S117	21	1	AND THE REAL PROPERTY OF THE PROPERTY OF	Esophageal	CR 54:2996
Unknown	D159118	17	1	0.05	Head&Neck	CR 54:1152
Unknown	D15S118	15	0	0.06	. Head&Neck	CR 54:4756
Unknown	D15S118	6	3	0	Head&Neck	CR 54:4756
Unknown	D15S120-D15S127	21	1	0.5	Kidney	GCC 12:76
Unknown	D15S120-D15S127	6	0	0.05	Kidney	PNAS 92:2854
Unknown	D15S28	18		0	Kidney	PNAS 97:2854
14-21	D1551	10	2	0.11	Kidney	CR 51:820
pter-q13	D15S24	26	1	0.1	Liver	JJCR 81:108
14-21	D1551	4	3 0	0.12	Liver	CR 51:89
14-21	D1551			0	Lung	NEJ 317:1109
14-21	D1551		0	0	Lung	PN 84:9252
14-21	D1551		2	0.4	Lung	NEJ 317:1109
Unknown	D15S28	2	0 2	0	Lung	NEJ 317:1109
Unknown	D15528	18		0.11	Lung	CR 52:2478;
14-21	D155118	24	4 0	0.17	Melanoma	CR 56:589
	01391	1	U	0	Neuroblasto	m CR 49:1095%
	•				a	

Chromosome 15 - q Arm

11-12.0	D15S11	13	1	0.08	Ovary	
Unknown	D15S2	11	4	0,36	The second secon	IJC 54:546
pter-q13	D15S24	31	?		Ovary	CR 53:2393
Unknown	D15S28	9		0.06	Ovary	IJC 54:546
26.1	FES			0.11	CASIA	CR 51:5118
pter-q13	*****	15	6	0.4	Ovary	BJC 69:429
	D15824	l	0	. 0	Pancreas	CR: 54:2761
Unknown	D15S29-D15S1	9	0	0	Prostate	G 11:530
14-21	D1591	9	4	0.44	Sarcoma	****
Unknown	D15S27	12	5	0.42		CR 52:2(19
14-21	D15S1	13		***************************************	Sarcoma	CR 52:2419
Unknown	D15S86	32		0	Stomach	CR 48:2988
pter-q13	D15824	CONTRACTOR CONTRACTOR	5	0.16	Stomach	HG 92:244
Unknown	The same of the sa	46		0.09	Testis	0.9:2245
222222222222222222222222222222222222222	D15586	21	2	0.1	Testis	GCC 13:249
Unknown	CYP19	27	0	0	Uterus	CR 54:4294
14-21	D15S1	6	1	0.17	The state of the s	The same of the sa
26.1	FES	36		***************************************	Uterus	CR 51:5632
SUM		1015	173	0;14	Oterus	CR 54:4294
		1013	173	0.17		

Chromosome 16 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	_	
13.3	HBZP1	6		0	Tumor Type	Refe
13.3	D16S85	7	0	0	Prostate	G 1
13.3	D16S85	62	5	0.08	Breast	CR
13.3	D16S85	8	0	0.08	Breast	GCC '
13:3	D16985	11	0	0	Liver	BJC
13.3	D16S85	24	5	0.21	Liver	BJC
13,3	D16585	11		0.21	Ovary	CR
13.3	D16S85	11	1	0.09	<u>Pancreas</u>	BJC
13.3	D16585	22	3	The state of the s	Stomach	HG
13.3	D16583	27	8	0.16	Testis	GCC
13,3	D16SB3	31	6	0.3	Breast	GCC
13.3	D16S83	16	2	0.19	Breast	CR
13.3	D16883	11	0	0.12	Esophageal	CR
13.3	D16583	19	5		Esophageal	CR.
13.3	D16583	16	-	0.26	Liver	CR
13.3	D16S83	15	6	0.06	Liver	CR
13	D16584	21	1	0.4	Sarcoma	CR
13	D16S84	43	0	0.05	Breast	CR
pter-pl3.3	D16584	5	0	0	Breast	CR
pter-p13.3	D16584	28	4	0	Cervix	GCC
pter-pl3.3	D16884	14	1	0.14	Esophageal	GCC
pter-pl3.3	D16S84	22	5	0.07	Kidney	CR
pter-p13.3	D16S84	21	7	0.23	Lung	CR
pter-pl3.3	D16S84	9	2	0.33	Ovary	CR
13.3	HBAT	22	5	0.22	Uterus	GCC
13.3	HBAI	47	1	0.23	Breast	CR
13.3	HBAI	22	5	0.02	Breast	CR
13.3	HBAI	11	9	0.23	Breast	CR
13.3	HBAI	36	16	0.82	Liver	CR
Unknown	D16S414	10	0	0.44	Liver	PNA
Unknown	D169414	19	3	0	Head&Neck	CR
Unknown	D16S414	6	3	0.16	Head&Neck	CR
Unknown	D16S414	26	ì	0.5	Kidney	GCC
13	D16S292	12	0	0.04	Melanoma	CR
pter-p13	D16S32	21	3,	0	Ovary	BJC
pter-p13	D16S32	26	8	0.14	Breast	CR
pter-pl3	D16532	16	4	0.31	Liver	PNA
pter-pl3	D16S32	8	7	0.25	Liver	JJC
13.1	MRP	13	5	0.88	Liver	CR
13.11	D16S131	8		0.38	Leukemia	LAN
13,11	D16S131	13	1 6	0.12	Breast	CR
12.2	D16S159	34	6	0.46	Liver	PNA
P11-P13	D168159	29	i i	0.18	Breast	CR
Unknown	D16S159	22	1	0.03		CR
Unknown	D16S159	22	1	0.05	Liver	CR
Unknown	Unknown	18	2	0.05	<u> Liver</u>	CR
		10	4	0.11	Brain	CR

Chromosome 16 - p Arm

12.2	D16S23	:36	5	0.14	Breast	CR
13.2	D16S34	3	1	0.33	Breast	CR
13.2	D16934	21.7	. 7	0.33	Breast	CR
PTER-P13	D16S35	26	4	0.15	Breast	CR
PTER-P13	D16S35	20	4 ;	0.2	Cervix	CR
12-pter	Unknown	18	0	0	Colon	BJC
Unknown	D168418	22	0	0	Endocrine -	2 CR
Unknown	D16S4O4	20	2	0.1	Head&Neck	CR
Unknown	D16S404-D16S403-D16S414	_22	0	0	Kidney	PNA
Unknown	D16S404-D16S403-D16S414	6	0	0	Kidney	PNA
13.2	D16534	20	9	0.45	Liver	PNA
13.2	D16S34	8	5	0.62	Liver	CR
13.2	D16S34	· . 6	3	0.5	Liver	CR
PTER-P13	D16535	7	4	0.57	Liver	CR
PTER-P13	D16535	24	9	0.38	Liver	PNA
pter-pl3	D16S37	2	0	0	Liver	JJC
13.2	D16534	27	4	0.15	Ovary	IJC
PTER-P13	D16S35	8	0	0	Prostate	PNA
PTER-P13	D16835	8	0	0	Prostate	CSu
12-pter	Unknown	5	0	0	Stomach	BJC
PTER-P13	D16535	25	5	0.2	Testis	0.9
Unknown	D16S291	18	1	0.06	Uterus	CR
SUM		1231	213	0.17		

Chromosome 16 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
16	D16S137	37	5	0.14	Breast	CR 54:513
Unknown	D16S300	23	ל	0.3	Breast	GCC 14:171
Unknown	D168299	36	7	0.19-	Breast	GCC 14:171
12.1	D16S304	24	12	0.5	Breast	GCC 14:171
22.1	TAT	43	16	0.37	Breast	CR_54:513
22.1	TAT	41	15	0.37	Breast	GCC 9:101
22.1	TAT	. 8	5	0.62	Liver	CR 52:1504%
22.1	TAT	10	9	0.9	Liver	CR 54:281
22.1	TAT	23	13	0.57	Liver	PNAS 87: 6791
22.1	TAT	25	13	0.52	Liver	PNAS 87:6791
22.1	TAT	29	14	0.48	Liver	PNAS 87, 6791
Unknown	D16S408	20	3	0.15	Breast	JJCR 86:1054
13	CET	36	9	0.725	Breast	CR 56:513 W -
21	CET	44	20	0.45	Liver	PNAS 87:6791
13-22.1	MT2	36	15	0.42	Liver	PNAS 87:6791
21	D16S151	43	16	0.37	Breast	CR 51:5794
21	D16S151	18	. 6	0.33	Breast	CR 54:513
21	D16S151	43	8	0.19	Esophageal	GCC 10:177
Unknown 21	D16S151	<u> </u>	2	0.25	Liver	CR 51:89
21	D16S265	70	24	0.34	Breast	GCC 9:101
21	D16S265	58	19	0.33	Breast	BCRT 32:5
22.1	D165265 D16538	19	3	0.16	Ovary	BJC 69:429
21-22.1	D16538	35	14	0.4	teeart	CR 54:513
21-22.1	D165186	28 33	15 13	0.54	Breast	GCC 14:171
21-22.1	D165186	27		0.39	Breast	GCC 9:101
22.1	D165318	33	6 13	0.22	Uterus	CR 54:4294
22.1	D165318	29	14	0.39 0.48	Breast	GCC 9:101
Unknown	D165421	12	2	0.17	Breast	GCC 14:171
Unknown	D16S421	27	14	0.17	Breast Breast	JJCR 8621054
22.1	D16S4	28	16	0.57	Breast	GCC 14:171 CR 54:513
22.1	D16S4	29	14	0.48	Breast	GCC 9:101
22.1	D16S4	31	12	0.39	Liver	PNAS 87:6791
22.1	D16S4	9	5	0.56	Liver	CR 52:1504
22.1	D1654	17	6	0.35	Ovary	CR 53:2393
22.1	D16S152	21	4	0.19	Breast	CR 54:513
22.1	НР	27	11	0.41	Breast	CR 54:513
22.1	HР	21	12	0.57	Breast	CR 51:5794
22.1	HP	29	15	0.52	Breast	GCC 9:101 %
22.1	HP	9	1	0.11	Cervix	CR 49:3598
22.1	HP	15	3	0.2	Colon	IJC 53:382
Unknown	HP	7	1	0.14	Liver	CR 51:89
Unknown	НР	10	. 4	0.4	Liver	CR:52:1504#
22.1	HР	28	10	0.36	Liver	PNAS 87:6791
22.1	HP	14	8	0.57	Liver	JJCR 81:108
22.1	HP	13	7	0.54	Liver	JJCR 81:108

Chromosome 16 - q Arm

22.1	HP	20	5	0.25	Lung	PN 84:9252
22.1	HP	4	0	0		om CR 49:1095
Unknown	HP	24		0.08	Ovary	GO 47:137
22.1	HР	22	5	0.23	Ovarv	IJC 54:546
22.1	#P	4	0	0	Prostate	G.11:530
Unknown	HP	11	1	0.09	Stomach	CR 52:3099
22.1	3 HP	10	0	• 0	Stomach	CR 48:2988
22.1	HP	2	0	0	Testis	CCG 52:72
22.1	THE	2	0	. 0	Testis	CCG 52:72
22.1	HP	2	0	0	Testis	CCG 52:72
22.1	HP	4	0	0	Oterus	CR 51:5632
22.3-23.2	CTRB	34	9	0.26	Breast	CR 54:513
23.2	- CTRB	4	2	0:5	Breast	7-7-7-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1
23.2	CTRB	9	5	0.56	Liver	CR 52:1504
22.3-23.2	CTRB	38 -	177	0:45	Liver	PNAS 87-6791
23.3-24.1	D16S289	28	13	0.46	Breast	GCC 14:171
23,3-24.1	D16S289	57	21	0.37	Breast	GCC 9:101-2
23.3-24.1	D16S289	22	5	0.23	Uterus	CR 54:4294
24.2	D16920	45	.15	0.33	Breage	CR 54:513
22.1-24	D16530	6	3	0.5	Breast	CR 54:513
Unknown	D1.6S511	32	15	0.47	Breast	GCC 14:171
Unknown	D16S402	12	5	0.42	Breast	JJCR 86:1054
Unknown	D165402	38	20	0.53	Breast	GCC 14:171
Unknown	D16S402	13	2	0.15	Head&Neck	CR 54:1152
24,2-24.3	D16S157	21	9	0,43	Breast	CR 54:513
22-23	D16S157	9	4	0.44	Breast	CR 51:5794
24.2-24.3	D16543	20	8	0.4	Breast	CR 54:513
Unknown	D16S155	11	2	0.18	Breast	CR 54:513
23-24	D16S156	61	30	0,49	Breast	CR 51:5794
24	APRT	33	17	0.52	Breast	CR 54:513
24	APRT	25	3	0.12	Breast	CR 53:3707
24	APRT	25	3	0.12	Breast	CR 53:4356
24	APRT	19	10	0.53	Breast	GCC 2:191
24	APRT	12	7	0.58	Breast	GCC 9:101
24	APRT	10	6	0.6	Liver	CR 52:1504
24	APRT	26	17	0.65	Liver	PNAS 87:6791
Unknown	D1697	10	1	0.1	Brain	CR 49:6572.
24	D1657	21	3	0.14	Brain	CR 50:5784
24	D1657	42	19	0.45	Breast	CR 50:7184
24	D16S7	8	6	0.75	Breast	CR 53:3804
24	D1697 -	354	164	0.46	Breast	BJC 71:438
24	D16S7	59	30	0.51	Breast	GCC 9:101
24	D1687	57	18	0:32	Breast	CR 53:4356
24	D16S7	57	18	0.32	Breast	CR 53:3707
24	D1697	269	120	0.45	Breast	C 74:2281
24.3	D16S7	68	32	0.47	Breast	CR 54:513
				0.47	Dreaze	CK 54:513

Chromosome 16 - q Arm

23-24	D1657:	138	59	0.43	Breast	CR 51:5794
Unknown	D1657	83	23	0.28	Breast	JJCR 84:1159
Unknown	D1697 ***	35	1	0:03	Cervix	CR 54:4481
23-24	D1657	7	2	0.29	Cervix	GCC 9:119
23-24	D1657	32	6	0.19	Colon	TUC 53:3823
23-24	D1657	6	1	0.17	Esophageal	CR 51:2113
Unknown	D1657	-15	4	0.27	Esophageal	CR 54-2996*
24	D16S7	29	3	0.1	Kidney	CR 51:820
Unknown	D1667	33	12	0:36	Liver	CR 51:89
24	D16S7	53	24	0.45	Liver	PNAS 87:6791
23-24	D1697	25	11	0.44	Liver,	CR 54:281
24	D16S7	50	14	0.28	Liver	JJCR 84:893
24	D1657	37	8	0.22	Lung	CR 52:2478
Unknown	D16S7	30	11	0.37	Ovary	CR 51:5118
24	D1697	3	i	0:33	Pancreas	CR 54:27613
24	D16S7	15	4	0.27	Prostate	PNAS 87:8751
Unknown	D16S7	17	3	0.18	Prostata	BJU 731390
24	D16S7	32	9	0.28	Sarcoma	CR 52:2419
24	D1697	43	2	0.05	Testis	0 9:2245
Unknown	D16S7	16	0	0	Uterus	GCC 9:119
24.3	D165413	41	21	0.51	Breast	GCC 14:171
24.3	D165413	22	0	0	Endocrine	CR 56:599
24.3	D16S44	10	4	0.4	Breast	CR 54:513
24.3	D165303	23	11	0.48	Breast	GCC 14:171
24.3	D165303	42	18	0.43	Breast	GCC 9:101
13	MT2	29	9	0.31	Breast	CR 54:513
13	MT2	в		0.5	Liver	CR 52:1504
13	MT2	8	4	0.5	Liver	CR 52:1504
Unknown	D16S10	31	7	0.23	Breast	GCC 9:101
Unknown	D165260	28	8	0.29	Breast	GCC 9:101
Unknown	D16S266	53	18	0.34	Breast	GCC 9:101
12.1	D16S27	26	7	0.27	Breast	CR 54:513
12.1	D16S27	27_	9	0.33	Breast	GCC 9:101
Unknown	D16S301	38	16	0.42	Breast	GCC 9:101
Unknown	D16S305	58	20	0.34	Breast	GCC 9:101
Unknown	D16S320	65	20	0.31	Breast	GCC 9:101
Unknown	D165398	56	16	0.29	Breast	GCC 9:101
Unknown	D16S5	29	11	0.38	Breast	GCC 9:101
. 22.1	E-cadherin	28	16	0,57	Breast	- GCC 9:101
22.1	E-cadherin	41	27	0.66	Breast	EMBO 14:6107
Unknowa	D165422	21	4	0.19	Read&Neck	CR 54:4756
Unknown	D16S422	20	0	0	Head&Neck	CR 54:4756
Unknown	SPN	22	: 3	0.14	Head&Neck	CR 54:1152
Unknown	D16S413-D16S402	21	0	0	Kidney	PNAS 92:2854
Unknown	D169419-D169402	- 6	Q	0	Kidney	PNAS 92:2854
Unknown	D16S:422-419	6	3	0.5	Kidney	GCC 12:76

Chromosome 16 - q Arm

Unknown	Unknown	3	. 0	0	Liver	BJC 67:1007
Unknown	Unknown	6	0	0	Liver	BJC 64:1083
Unkno₩n	D169:422-419	21	0	0	Melanoma	CR 56:589
Unknown	Unknown	16	5	0.31	Prostate	CSurveys 11:
MUE		4382	1588	0.36		

Chromosome 17 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
Unknown	D17534	35	- 5	0.14	Brain	AJP 145-11
13.3	D17S34	8.2	29	0.35	Breast	AJP 140:21
13.3	D17934 ··	77 😯	52	0.68	Breast	CR*54:4200
13-TER	D17S34	72	30	0.42	Breast	CGC 76:106
Unknown	D17534	70	41	0.59	Breast	0 8:781
13.3	D17S34	4 4	33	0.75	Breast	GCC 4:113
13,3	D17934	36	22	0.61	Breast	CR 53:1637
Unknown	D17S34	11	6	0.55	Cervix	CGC 79:74
13.3	D17834	68	34	0.5	Colon	EIC:304.66
13.3	D17S34	6	5	0.83	Colon	Science Ap 1989:217
13.3	D17834	6	3	0.5		AUR 14251.
Unknown	D17S34	12	1	0.08	Head&Neck	CR 52:4787
13.3	017934	20	2	0.1	Liver	O REACT:
13.3	D17S34	10	8	0.8	Liver	BJC 64:108
13.3	D17634	9:	4	0.44	Liver	31C (552.00)
13.3	D17S34	23	12	0.52	Ovary	IJC 54:85
13,3	D17834	20	18	0.9	Ovary	IJC/54:220
Unknown	D17S34	43	18	0.42	Ovary	CR 56:606
13.3	D17534	. 11	0	0	Pancreas	CR 54:2761
13.3	D17S34	17	3	0.18	Prostate	CSurveys 1
13.3	D17934	18	3	0.17	Prostate	PNAS 87:87
13.3	D17S34	7	5	0.71	Sarcoma	CR 53:468
13.3	D17534	9	0	0	Sarcoma	CR 53:468
13.3	D17S34	10	4	0.4	Sarcoma	CR 53:468
13,3	D17934	4	2	0.5	Sarcoma	CR 53:468
13.3	D17534	20	0	0	Testis	GCC 13:249
13.3	D175849	26	16	0.62	Breast	RMG 4:2047
13.3	D175926	12	7	0.58	Breast	HMG 4:2047
13.3	D17930	54	20	0.37	Breast	CR 53:1637
13.3	D17530	98	57	0.58	Breast	Lan 336:76
13.3	D17S30	59	30	0.51	Breast	JNCI 84:50
13.3	D17530	52	27	0.52	Breast	PNAS 88:38
13.3	D17930	51	8	0.16	Breast	HG 91:6.
13.3	D17530	34	16	0.47	Breast	CR 50:7184
13.3	D17530	33	17	0.52	Breast	ANYAS p.13
13.3	D17S30	3	0	0	Breast	CR 53:2947
13.3	D179 3 0	6	31	0.5	Cervix .	GCC \$9:119
13.3	D17S30	39	27	0.69	Colon	CR 50:7166
13.3	D17530	60	38	0.63	Colon	EJC 30A:66
13.3	D17S30	65	40	0.62	Esophageal	GCC 10:177
, 13.3	017930	51	36	0.71	Head&Neck	0 1051217
13.3	D17S30	5	2	0.4	Liver	BJC 67:100
13.3	D17530	26	16.	0.54	Liver	CR_51089
13.3	D17S30	37	23	0.62	Lung	CR 52:2478
13,3	D17830	16	4	0.25	Melanoma	GCC 7/169

Chromosome 17 - p Arm

13.3	D17S30	14	9	0.64	Ovary	CR 50:2724
13.3	D17530	21	19	0.86	Overy	IUC 54:85
13.3	D17530	46	37	0.8	Ovary	CR 56:606
13.3	D17830	(1	27	0.66	Ovacy	0.7:1059%
13.3	D17S30	7	0	0	Prostate	GCC 11:119
1373	@D17530.	-3	0	.0	Sarcoma	CR 533468
13.3	D17S30	6	4	0.67	Sarcoma	CR 53:468
13.3	E17530	37	0	0	Sarcoma	CR 53:468
13.3	D17S30	6	0	0	Sarcoma	CR 53:468
13.3	D17530	17	16	0.94	Sarcoma	CR 49:6247
13.3	D17S30	15	. 3	0.2	Uterus	GCC 9:119
13.3	017528	11	4	0.36	Brain	CR 49:6572
13.3	D17528	22	3	0.14	Brain	AJP 145:11
13.3	D17528	12	4	0.33	Brain	CR 493.6572
13.3	D17528	27	11	0.41	Breast	CR 54:6270
13.3	0)(7)(52)	62	15.	0.24	Breast	CGC 76-106
13.3	D17528	37	26	0.7	Breast	CR 54:4200
13.3	D17528	11	4	0.36	Breast	HMG 4:2047
13.3	D17S28	23	12	0.52	Breast	CR 53:1637
13,3	D17S28	27	4	0.15	Cervix	CR 54:4481
13.3	D17S28	14	1	0.07	Cervix	BJC 67:71
13.3	D17528	7	5	0.71	Colon	Science Ap
						1989:217
13.3	D17S28	13	8	0.62	Colon	GCC 3:468
13.3	D17528	12	4	0.33	Colon	CCG 48:167
13.3	D17S28	2	0	0	Head&Neck	CR 52:4787
13.3	D17528	11	0.	0	Kidney	JU 150:129
13.3	D17S28	3	1	0.33	Liver	CR 53:368
13.3	D17528	3	33	<u> </u>	Long	CR 49:5130
13.3	D17S28	16	2	0.12	Ovary	IJC 52:575
13.3	D17S28	8	<u> </u>	0.75	Ovary	CR 50:2724
13.3	D17528	23	15	0.65	Ovary	CR 56:606
13.3	D17528	6	4	0.67	Overy	IJC 54:85
13.3	D17S28	18	14	0.78	Ovary	IJC 54:220
13.3	D17S28	A STATE OF THE PARTY OF THE PARTY OF	1	0.33	Pancress	CR 54:2761
13.3	D17S28	3	0	0	Pancreas	GCC 3:468
13.3	D17528	10	22	0.2	Stomach	BJC 591750
13.3	D17S28	7	0	0	Stomach	HG 89:445
13.3	D17528	29	12	0,41	<u> Pestis</u>	0 9:2245
Unknown	D17S28	1 20	1	1	Uterus	CR 51:5632
Unknown	Unknown	- B- G- 1- 17 - C- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1-	10	0.5	Bladder	JU 153:109
13.3	Unknown D17534-55	76 13	21 7	0.28	Brain	CR 56:164
13.3	D17S34-S5	ALCONOMICS AND AND AND AND AND AND AND AND AND AND	A STATE OF THE PARTY OF THE PAR	0.54	Brain	CR 54:1397
13.3	D17534-55	20 22	11	0.55	Brain	CR 54:1397
13.3	D17S5	2		<u>0.18</u> _	<u>Brain</u>	AJP 145:11.
13.3	D1755	16 13	6 6	0.36	Brain	IJC 63:372
	94/33		TO .	0.46	.Brain.	CR 49:6572

Chromosome 17 - p Arm

13.3	D1785	11	6	0.55	D	
13.3	Unknown	72	20	0.33	Brain Breast	CR 49:6572
13.3	D1785	62	26	0.42		AJP 140921
13.3	D1755	68	37	20.54	Breast	JJCR 84:11
13.3	D17S5	57	28	0.49	-Breast	0.8.781
13.3	D1785	4	2	0.19	Breast Breast	BCRT 28:23 CR 53:3804
13.3	D17S5	29	16	0.55	Breast	GCC 2:191
13;3	D1755		8		Breast	CR 53:4356
13.3	D17S5	465	224	0.48	Breast	BJC 71:438
13.3	D1785	34	. 15	0.44	Breast	BMG 4 2017
13.3	D17S5	82	53	0.65	Breast	CR 54:4200
13,3	D1755	75	21	0.28	Breast	CGC 76:106
13.3	D17S5	354	174	0.49	Breast	C 74:2281
13.3	:D1795	39	18	0.46	Breast	100.53101
13.3	D17S5	42	25	0.6	Breast	IJC 50:528
13.5	D1765	1015	27	***************************************	Breast	GCC 4 (113
13.3	D17S5	125	63	0.5	Breast	CR 51:5794
13.3	01785	61	26	0.43	Breast	BG 90:635
13.3	D17S5	52	27	0.52	Breast	PNAS 88:38
13.3	D1765	15	4	0.27	Cervix	CGC 79:74
13.3	D17S5	12	1	0.08	Cervix	BJC 67:71
13.3	01785	32	5	0.16	Cervix	CR 5424481
13.3	Unknown	7	6	0.86	Colon	Science Ap
				0.00	C010!!	1989:217
13.3	D1785	35	26	0.69	Colon	BJC 59:750
13.3	D17S5	19	7	0.37	Colon	CCG 48:167
13.3	D1755	5	3	0.6	Colon	O 9:991
13.3	D17S5	27	21	0.78	Colon	IJC 53:382
13.3	01755	17	7	0.41	Colon	GCC 3:468
13.3	D1755	26	10	0.38	Colon	5 241:961
	D17934-S5	24	11	0,46	Esophageal	CR 52:6525
13.3	D17S5	22	10	0.45	Esophageal	CR 51:2113
13.3	Unkaown	6	5	0.83	Bead&Neck	AJP 142111
13.3	D17S5	11	2	0.18	Head&Neck	CR 52:1494
13.3	<u> D1755 </u>	48.	8	0,17	Kidney	CR 51:5817
13.3	D17S5	23	6	0.26	Kidney	JU 150:129
13.3	<u>017\$5</u>	15	5	0.33	Kidney	CR 51;820
13.3	D17S5	31	5	0.16	Kidney	CR 51:1544
13.3	D17\$5	15	1	0.07	Kidney	CR 51:1071
13.3	D17S5	2	1	0.5	Kidney	CR 51:1544
13.3	01755	20	3	0,15	Liver	0 8:491
13.3	D17S5	14	3	0.21	Liver	CR 51:4367
13.3	D1755	33	15	0,48	Liver	CR: 53:368
13.3	D1785	9	3	0.33	Liver	BJC 64:108
13.3	D17834-85	-11	11		Lung	CR 49;5130
13.3	D1755	6	6	1	Lung	CR 55:28
13,3	P17834-85	.38	25	0.66	Oyary.	0.7:2069

Chromosome 17 - p Arm

13.3	13.3	D17S34-S5	6	2	0.33	Ovary	0 7:2069
13.3	13.3	D1785	17	13		Transmitted to the second	
13.3	13.3	D17S5	28	12	0.43		
13.3	·	D1755		9	0.27		
13.3	VVIII.	***************************************	34	7	0.21		
13.3			2/10/2	27	0.66		
13.5		***************************************	28		0.54		
13.3	The second secon		5	0		Рапокевя	MC2200000000000000000000000000000000000
13.3	***************************************				0	Pancreas	BJC 65:809
13.3 DITSS 22 16 0.73 Salcoma CGC73345 13.3 DITSS 22 16 0.73 Salcoma CR 52:2419 13.3 DITSS 38 19 0.5 Stomach CR 51:2926 13.3 DITSS 38 19 0.5 Stomach CR 51:2926 13.3 DITSS 24 9 0.38 Stomach CR 51:2926 13.3 DITSS 39 0.78 Stomach CR 51:2926 13.3 DITSS 24 9 0.38 Stomach CR 51:5632 13.3 DITSS 9 4 0.44 Userus CR 51:5632 13.3 DITSS 9 4 0.44 Userus CR 51:5632 13.3 DITSS 9 4 0.44 Userus CR 51:5632 13.3 DITSS 9 6 0.21 Ovary CR 56:606 DENROWN DITSSS 16 10 0.62 Breat CR 54:4200 13 DITSS 2 2 1 0.69 Breast GE 5:554 13 DITSS 15 3 0.2 Breat CR 54:4200 13 DITSS 15 3 0.2 Breat CR 54:4200 13 DITSS 15 3 0.2 Breat CR 54:4200 13 DITSS 15 3 0.2 Breat CR 54:4200 13 DITSS 15 3 0.2 Breat CR 54:4200 13 DITSS 15 3 0.2 Breat CR 54:4200 13 DITSS 15 3 0.2 Breat CR 55:554 13 DITSS 15 2 0.19 Breat CR 54:4200 13 DITSS 20 9 0.60 Breast CR 53:4356 13 DITSS 20 9 0.60 Breast CR 53:4356 13 DITSS 3 0 0 0 0 0 0 0 0 13 DITSS 3 0 0 0 0 0 0 0 0 13 DITSS 3 0 0 0 0 0 0 0 0 13 DITSS 3 0 0 0 0 0 0 0 13 DITSS 3 0 0 0 0 0 0 0 13 DITSS 3 0 0 0 0 0 0 0 13 DITSS 3 0 0 0 0 0 0 0 13 DITSS 3 0 0 0 0 0 0 13 DITSS 3 0 0 0 0 0 0 14 DITSS 3 0 0 0 0 0 0 15 DITSS 3 0 0 0 0 0 0 16 DITSS 3 0 0 0 0 0 17 DITSS 3 0 0 0 0 0 18 DITSS 3 0 0 0 0 0 19 DITSS 3 0 0 0 0 0 10 DITSS 3 0 0 0 0 0 11 DITSS 3 0 0 0 0 0 12 DITSS 3 0 0 0 0 0 13 DITSS 3 0 0 0			***************************************	. 2	0.00	□Pan -, c aai/s	160031752061
13.3	A-V	* : 100000000000000000000000000000000000		************	****	Pediatric	CR 50:3279
13.3	CANADA MANAGEMENT OF THE PROPERTY OF THE PROPE					Sarcona	GGC#58.45
13.3	V/4044444444444444444444444444444444444				99732228309240P0000000000000000000000000000000000	P72010 00070 00010 0000 00000 00000	***************************************
13.3 D1755 24 9 0.38 Stomach RC 92:244							
13.3 D1755 24 9 D.38 Stomach HG 92:244 11.3 D1755 9 4 D.2 Test15 D.972265 13.3 D1755 9 4 D.44 Uterus CR 51:5612 13.3 D175379 22 15 D.65 So Ovary CR 56:606 13.3 ABR 29 6 D.21 Ovary CR 56:606 D1000000000000000000000000000000000000		***************************************	***************************************	***************************************			
13:3					The second secon		
13.3	**************************************		***************************************				
13:3 D175379 22 15 0.68 Ovary CR 51:5632	· · · · · · · · · · · · · · · · · · ·						
13.3 ABR 29 6 0.21 Ovary CR 56:606 Onknown D17665 16 10 O.62 Breast CR 54:4200 13 D17865 16 11 0.69 Breast GE 5:554 13 D17865 2 2 1 Cclon SiApril 16 13 D1751 15 3 0.2 Brain AJP 145:11 14 D1781 15 2 D.13 Brain AJP 145:11 13 D1781 20 9 0.45 Breast HG 91:6 13 D1781 20 9 0.45 Breast GCC 2:191 13 D1781 29 9 0.31 Breast CR 53:4356 13 D1781 29 9 0.31 Breast CR 53:4356 13 D1781 29 9 0.31 Breast CR 53:4356 13 D1781 24 0.43 Colon CR 50:7166 13 D1781 2 2 2 1 Colon SiApril 16 13 D1781 2 2 2 1 Colon SiApril 16 13 D1781 2 2 2 1 Colon SiApril 16 13 D1781 12 2 4 0.33 Colon CR 53:436 13 D1781 12 2 4 0.33 Colon SiApril 16 13 D1781 12 2 4 0.33 Colon SiApril 16 13 D1781 12 2 4 0.33 Colon SiApril 16 13 D1781 3 1 0.16 Liver JUCR-81:10 13 D1781 3 D1	*********************************	((2000000000000000000000000000000000000	-			******************************	
District	13.3						······································
13	Unknown				**************************************	*****************	
13		AND DESCRIPTION OF PERSONS ASSESSMENTS					
13		D17565	2 * 1	***************************************	~~~~	2002/01/10/10/10/10/10/10/10/10/10/10/10/10/	
13		D17S1	15	3	0.2		
13	13	01781	15	2	****	********************************	***************************************
13		**********	21				
13 D17S1 29 9 0.31 Breast CR 53:4356 13 D17S1 14 6 0.43 Colon CR 50:7166 13 D17S1 9 0 0 0 Colon N 331:275 13 D17S1 12 4 0.33 Colon S:April 16 13 D17S1 12 4 0.33 Colon S:April 16 13 D17S1 30 13 0.43 Head\$Neck 0 10:1217 13 D17S1 30 13 0.43 Head\$Neck 0 10:1217 13 D17S1 11 2 0.14 Liver JJCR.B.110 13 D17S1 11 2 0.18 Liver CR 53:368 13 D17S1 9 8 0.89 Lung PNAS:86:50 13 D17S1 9 8 0.89 Lung PNAS:86:50 13 D17S1 7 7 1 Lung CR 49:5130 13 D17S1 17 8 0.47 Lung PNAS:86:50 13 D17S1 1 2 0.18 Liver PNAS:86:50 13 D17S1 1 2 0.89 Lung PNAS:86:50 13 D17S1 1 2 0.89 Lung PNAS:86:50 13 D17S1 1 2 0.89 Lung PNAS:86:50 13 D17S1 1 2 0.89 Lung PNAS:86:50 13 D17S1 1 2 0.89 Lung PNAS:86:50 13 D17S1 1 2 0.89 Lung PNAS:86:50 13 D17S1 3 1 0.83 Sarcoma CR 49:1095 a	13	D1751	20	9	0.45	Breast	GCC 2:191
13			29	9	0.31	Breast	
13	Commence of the Commence of th			2	0.29	Cervix	CR 49:3598
13			~~~~		0.43	Colon	CR 50:7166
13					A CONTRACTOR OF THE PARTY OF TH	Colon	N 331(215)
13		***************************************		******************************		***************************************	
13				THE RESERVE THE PARTY OF THE PA			
13	***************************************	***************************************					
13 D17S1 3 1 0.33 Lung PNAS/86150 13 D17S1 9 8 0.89 Lung PNAS/86150 13 D17S1 9 8 0.89 Lung PNAS 86:50 13 D17S1 17 3 0.47 Lung PN 84:9252 13 D17S1 7 7 1 Lung CR 49:5130 13 D17S1 14 0 0 Neuroblastom CR 49:1095 14 D17S1 5 0 0 Sarcoma CR 53:468 13 D17S1 3 1 0.33 Sarcoma CR 53:468	A CONTRACTOR OF STREET, STREET	A AND DESCRIPTION OF THE PROPERTY OF THE PAR					***************************************
13 D1751 9 8 0.89 Lung PNAS 86:50 13 D1751 17 8 0.47 Lung PN 84:9252 13 D1751 7 7 1 Lung CR 49:5130 13 D1751 4 0 0 Neuroblastom CR 49:1095 13 D1751 4 0 Sarcoma CR 53:468	V-WARRANCE MARKET AND A STREET					CONTRACTOR STATE OF THE STATE O	
13	The state of the s			AND RESIDENCE AND ADDRESS OF THE PERSON OF T			
13					PC 4577475 VIVINIA PROFESSOR PROFESSOR PROFESSOR PROFESSOR PROFESSOR PROFESSOR PROFESSOR PROFESSOR PROFESSOR P		
13	11. (1mm) 11. (1		THE PERSON NAMED IN COLUMN 2 I		AND DESCRIPTION OF A SPECIAL PROPERTY OF SPECI		
13 D1751 4 0 0 Neuroblastom CR 49:1095 a 13 D1751 5 0 0 Sarrowg CR 53:668% 13 D1751 3 1 0.33 Sarrowa CR 53:468	13	·			*****	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
13 D17S1 5 0 O Sarcomg CR 53:468) 13 D17S1 3 1 0.33 Sarcoma CR 53:468	COMPANY OF THE PROPERTY OF THE PARTY OF THE		And to see the second second				
13 D17S1 3 1 0.33 Sarcoma CR 53:468	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX			-		a	
1 0.55 Salcoma CR 55:406	· · · · · · · · · · · · · · · · · · ·	The second of th		0	0	Sarcona	CR 53; (68)
13. D175) 3 0 0 SATCOMB CR 53:468	CONTROL CONTRO			***************************************	0.33		
	13	D1751	*3 **	<u> </u>	9	Sattoma	ÇR 537460

Chromosome 17 - p Arm

13	D17S1	8	7	0.88	Sarcoma	CR 52:2419
13	and Comment	7		0.00	Sarcona	819 (C-710/1)
13	D17S1	13	12	0.92	Sarcoma	CR 49:6247
15				0.2534	Stomach	AGE 57 (41099)
13	D17S1	10	0	0	Stomach	CR 48:2988
13 /4	and the state of	tead at		0.0716	Uterios	CR 53-55-72
Unknown	D17S796	17	0	0	Endocrine	CR 56:599
Unknown	(107 6941672)	- 11		0.410	Haad&Neck	CR05#24786
Unknown	D175796	33	0	0	Head&Neck	CR 54:4756
Doknown	a divisibles	6	3 1	0.5	Kudney	TEGORALIZATION
Unknown	D175796	32	5	0.16	Melanoma	CR 56:589
12.0-13	0175906	19	3	0.16	Prostate :-	2(C60 312)(27F)
13.1	D17S31	9	2	0.22	Brain	CR 49:6572
13.1	EVADA (FILLE)		2/92	0.2/07/2004/1994/2	CONTRACTOR CONTRACTOR	Some Carlo
13.1	D17S31	8	4	0.5	Brain	CR 49:6572
15.1	ROMANIA STATE	11		(0.4E)	Bretast	\$9:{e=65:265:75
13.1	D17S31	54	24	0.44	Breast	Lan 336:76
13-1	D17531	100	22	0.65	Breast	GR 51 4 (200)
13.1	D17S31	87	37	0.43	Breast	CR 51:5794
13,1-11.2	D17931	25	14	0.44	Breast	TJC 50/528
13.1	D17S31	2	1	0.5	Breast	CR 53:2947
13.1	D17531	11		0.09	Cervix.	BUC 671/11
13.1-11.2	D17S31	16	7	0.44	Colon	CR 50:7166
13.1	D17831***	6			Colon	5:Aprilile
13.1	D17531	15	9	0.6	Esophageal	CR 54:2996
13.1	D17531	. 29	1.8	0.62	BeadsNeck	0.10:1217
13.1-11.2	D17531	28	5	0.18	Kidney	CR 51:5817
13.1	017831	25	0	0	Kidney	JU 150:129
13.1-11.2	D17S31	16	6	0.38	Liver	CR 51:89
13.1	D17531	. 21	12	0.57	Liver	CR 531368
13.1	D17531	17	7	0.41	Ovary	IJC 54:546
13.1	D17531	7	2	0.29	Ovary	TJC 54:85
13.1	D17S31	11	8	0.73	Ovary	IJC 54:220
13.1	017531		4	0.57	Ovary	BJC 65:40
13.1	D17S31	6	2	0.33	Ovary	CR 56:606
13.1	017531	3	<u> </u>	0.33	Pancress.	CR 542-2761
13.1-11.2	D17S31	17	12	0.71	Sarcoma	CR 52:2419
13.1	D17531 :	15	15	1	Sarcoma	CR 49.6247
13.1	D17531	12	9	0.75	Sarcoma	CR 52:2419
13.1	TP53		0	0	Bladder.	HG 91 (455
13.1	TP53	21	9	0.43	Brain	CR' 54:1397
	TP53	1	0	0	Brain	AUR 145111
13.1	TP53	45	6	0.13	Brain	0 6:1313
<u>* 13,1</u>	TP53	. 6	2	0,33	<u>Braio</u>	CR 49:6572
13.1	TP53	22	9	0.41	Brain	CGC 74:139
13.1	TP53	-38	11	0,29	Brain	CR 52:1427

Chromosome 17 - p Arm

13.1	TP53	15	7	0.47	Design	
13.1	TP53	6.5	,		Brain	CR 54:1397 CR 49:6572
13.1	TP53	31	22	0.71	Breast	
Unknown	TP53	63	17	27748C0077974000070070707070707070707070707	Breast	BJC 68:64
13.1	TP53	61	14	0.23	Breast	
Daknown	TP53	19	6	0.32	Breast	CGC 76:106
13.1	TP53	4.4	28	0.64	Breast	
13.1	TP53^	35*	-13	0.37	Breast	HG 90:635
13.1	TP53	70	26	0.37	Breast	CR 51:5794
13.1	TVP53	65	13	50.7	Breast	CR 31:3794
Unknown	TP53	11	6	0.55	Breast	CR 52:2624
13.1	TP53	81	22	0:27	Breast	Lau: 33.6276
13.1	TP53	25	10	0.4	Breast	GCC 4:113
13.1	TP53	36	10		8reast	BUC 4:113
13.1	TP53	12	5	0.42	Breast	CR 53:2947
13.1	7(253	110	72	0.65	Breast	CR 54:4200
13.1	TP53	36	15	0.42	Breast	CR 53:1637
13.1	TP53	17	9	0.53	Breast	GCC.42.113
13.1	TP53	41	34	0.83	Breast	IJC 57:498
Unknown		16	0	0	Cervix	CGC=79:74
13.1	TP53	9	1	0.11	Cervix	BJC 67:71
Daknown	TP53	6	3	0.5	Cervix	GCC 9:119
13.1	TP53	21	5	0.24	Cervix	CR 54:4481
13.1	TP53	17	β	0.47	Colon	CR 52:741
13.1	TP53	6	5	0.83	Colon	GAST 107:3
Unknown	TP53	23	15	0.65	Colon	EJC 30A:26
Unknown	TP53	48	38	0.79	Colon	0 8:1391
Unknown	TP53	26	22	0:85	Colon	GAS 103:16
13.1	TP53	30	17	0.57	Colon	GAST 104:1
Unknown	TP53	. 6	4	0.67	Colon	0.9:991
13.1	TP53	25	12	0.48	Colon	HP 25:1069
13.1	TP53	14	<u> </u>	0.57	Colon	CR 50:7166
13.1	TP53	17	8	0.47	Colon	JNCI 84:11
13.1	TP53	17	?	0.41	Colon	JNCI 84:11
13.1	TP53	17	10	0.59	Colon	IJC 53:382
13.1	TP53	25	14	0.56	Colon	CR:52:3965
13.1 13.1	TP53	12	10	0.83	Colon	CR 51:4436
The state of the s	TP53	27	15	0.56	Esophagea	1
13.1	TP53	14	10	0.71	Esophagea	1 C 71:1933
Unknown	TP53	47	27	0,57	Esophagea	L CR 52:6525
13.1	TP53	14	7	0.5	Head&Neck	CR 54:1152
Unknown		32	14	0.44	-Read&Neck	0 9:2077
13.1 13.1	TP53	27	15	0.56	Head&Neck	
13.1	TP53	39	21	0,54	Heads Neck	0 10:1217
Unknown	TP53	20	4	0.2	Kidney	CR 51:5817
onvito Mil	TP53	40	5	0.12	Kidney	BUC 691230

Chromosome 17 - p Arm

13.1	mn = 2					
13.1	TP53	2	0	0	Kidney	GCC 12:76
13.1	TP53	10		0.6	Kudney	IJC 64(899
Unknown	TP53	16	3	0.19	Kidney	CR 51.820
13.1	TP53	65 50		0.16	Leuken a	B 86 (587)
	1955	50	14	0.28	Liver	JJCR 84:89
Unknown	TP53	4	6		e de la cretta de la	0.00 CR (5) (45520)
13:1		•	1	0.25	Liver	CARC 17:14
Unknown	TP53	19		10,58	Liver	C TELLIPS
713.1	7255	5	11	0.58	Liver	CR 54:281
13.1	TP53	7		0.8	Liver	0.0 2303
13.1	TP53	24	3 17	0.43	Liver	CR 51:89
13.1	TP53	57		0.71	Lung	CR 54%5643
13/1	7953	5 /	21	0.37	Lung	0 10:937
13.1	TP53	3			Salarity Salar	9.641.517.6
13-1	0.05		2	0.67	Lung	CR 54:5643
Unknown	TP53	28			A Parental	GCC 778169
13.1	77559	42	7	0.25	Melanoma	PJC 69:253
13.1	TP53	12		0.45	Overy	CR 561606
13.1	TP53	18	5 2 10	0.42	Ovary	IJC 54:546
13.1	TP53	9		0.56	Ovacy	BJC 65:40
13.1	TP53	9	6 2	0.67	Ovary	IJC 54:85
13.1	TP53	23		0.22	Ovary	IJC 52:575
13.1	TP53	18	18	0.78	Ovary	IJC 54:220
13.1	TP53	12		0,67	OvatA	BJC 69:429
13.1	TP53	20	3	0.25	Ovary	CR 51:5118
Unknown	TP53	35	16	0,8	Ovary	CR 51:5171
13.1	TP53	7	26	0.74	Ovary	BJC 72:883
13.1	TP53	2	1	0.14	Ovary	0 7:2069
13.1	TP53	32	1 18	0.5	Ovary	0 7:2069
13.1	TP53	13	3	0.56	Cyary	0 7:2069
13.1	TP53	7	'S	0.23	Ovary	0 7:2069
13.1	TP53	27	3	0.71	Pancreas	GCC 15:157
13.1	TP53	8	3	0.11	Prostate	AJP 145:28
13.1	TP53	4	0	0.38	Prostate	JU 151:107
Unknown	TP53	. 5	3	0	Prostate	AJP 147:11
Unknown	TP53	4		0.6	Sarcoma	CR 531468
Daknown	TP53	7	1	0.25	Sarcoma	CR 53:468
Unknown	TP53	12	***************************************	0.14	Sarcoma	CR 53:468
Unknown	TP53	63	6 23	0.5	Sarcoma	CR 53:468
13.1	TP53	16	5	0,37	Stomach.	LI 72:232
Doknown	TP53	5	5	0.31	Stomach	CGC 75:45
13.1	TP53	7		0.2	<u>Testia</u>	GCC 6:92
13:1	TP53	9	3	0.43	Testis	0 9:2245
13.1	TP53	3	*******	0,22	Uterps	GCC 9:119
13.1	TP53	- i	1	0.33	Uterus	CR 51:5632
			<u> </u>	0.25	Oterus	CR-51:5632

Chromosome 17 - p Arm

Unknown	TP53	28	-			
13:17	D175786	25	3	0.11	Uterus	CR 54:4294
13.1	D17S786	2		0.15	Cervix	GR/5503(9)
12	D178520°	2	0	0	Kidney	GCC 12:76
12	D17S520			0.5	Bralb	CRU54 (1597)
13 17	D173320	20	13	0.65	Brain	CR 54:1397
12	D17S520			10000	Head (Neck	0.00
13 1 2 2	D173520	19	11	0.58	Ovary	BJC 69:429
13.1	MYH2	26		0.08	Uterus	CR\S164Z94
1.3	77.00 27.77 CO. CO. CO. CO. CO. CO. CO. CO. CO. CO.	10	5	0.5	Brain	CR 49:6572
13.1	MANS	- 8		0.25	Brain	CR249:6572
13.1	MYH2	14	1	0.07	Brain	
13.1	MXE2	14	10	0.71	Colon	AJP 145:11
13.1	MYH2	5	2	0.4	Liver	1002537362
	MYH2	10.5		0.7	in ver	CR 53:368
13.1	MYH2	10	10	1	Lung	0.00
	MYB2	16	*****		Overv	CR 49:5130
13.1	MYH2	15	12	0.8		NO 51636
13.1	MYH2	12	6	0.5	Sarcoma	CR 49:6247
13.1	MYH2	19	8	0.42	Sarcoma	CR-52:2419
13:1	MYB2	20.	6	0.42	Stomach	CR 52:3099
12	D17567	8	4	0.5	Vterus	CR 5153632
12	D17567	35	22		Brain	AJP 145:11
12	D17S67	12	11	0.63	Breast	CR 5414200
12	D17567	1	1	0.92	Breast	GE 5:554
			•	1	Colon	Science: Ap
12	D17S67	22	10	0.45	^	1989:217
12	017867	16		0,44	Ovary	IJC 54:546
13.1	EW505	3	2	0.67	Ovary	CR_56:606
	***************************************		_	0.67	Colon	Science Ap
13.1	UC 10-41	4.	3	0.75	Colon	1989:217
13.1		<u></u>			coton.	Science Ap
13.1	EW401	3	1	0.33	Colon	1989:217 Science Ap
13.1			***************************************			1989:217
	EW402	2	1	0.5	Colon	Science: Ap
13.1	EW405					1989:217
***************************************	211103	3	1	0.33	Colon	Science Ap
13.1	D17829	15	1			1989:217
13.1	D17S29	9		0.07	Brain	CR 49:6572
13.1	D17529	2	0	0.11	Brain	CR 49:6572
		-	U	0	Colon	Science«Ap
13.1	CHRNB1	26	14	2.5.		1989:217
13.1	CHRNEI	22	E	0.54	Head&Neck	0 9:2077
13.1	CHRNB1	28	14	0.36	Sead SNeck	CR 5491152
11,2-12	D175261	6	2	0.5	Ovary	CR 56:606
11.2-12	D17S261	7	3	0.33	Brain	CR 54 (1397)
11.2-12	D178261	19	8	0.43	Brain	CR 54:1397
12-11.2	D17S71	15	2	0:42	Lenkemia	B.83:3 449
		13	4	0.13	Brain	AJP 145:11

Chromosome 17 - p Arm

12-11-2						
12-11.2		3	2	(947)		V-10-36-11-66-8
12-11-2	D17S71	18	15	0.83	Colon	T.TC 53.300
12-11.2				CONTRACTOR AND A SECOND	Sept. Sept.	(4) (4) (4) (4) (4) (4) (4) (4) (4) (4)
12-11-2	D17S71	10	10	1	Lung	C.D. Line and C. L. Control of the C
12-11.2		2500 61 200			Security of the Control of the Contr	CK 43:5130
12-11:2	D17S71	20	++	0.55	Ovary	GO 47:137
12-11.2	01/5715	1/2	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	retrained to the	M. G. Transmission	60 47:137
12-11.2	D17S71	9	5	0.56	Sarcoma	
13.1	p17971			(14 (14 (14 (14 (14 (14 (14 (14 (14 (14	A PROPERTY OF	CR 52:2419
13.1	D17S122	23	4	0.17	Brain	The second secon
13.1	-0179127	29		0.00	Beachwark	AJP 145:11
	D175122	12	7	0.58	Head&Neck	
Üüknown		19975			Headaneck	CR 54:1152
11.2-11.1	D17S58	21	7	0.33	Breast	0.2
11.7	017558	L (*)-	**.*F**	William Committee of the Committee of th	Break	GE 5:554
Unknown	D17S58	35	14	0.4	Breast	The state of the s
11.2-11.1	0.066	2536			Wines.	0 8:781
11.2~11.1	D17S58	5	1	` 0.2		The control of
				0.2	Colon	Science Ap
Unknown	D17958	9	0	0	HeadsNeck	1989:217
11.2-11.1	D17S58	11	9	0.82	Ovary	
Unknown	D17558	19	12	0.63	Ovary.	IJC 54:85
Unknown	D1721	27	1	0.04	Breast	CR 56:606
Unknown	D17Z1	27	L I	0.04	Breast	GE 5:554
D17S5-D17S58	Unknown	21	8	0.38	Bladder	
Unknown	CHRNB14TP53	30	18		Bladder	CR 51:5405
Unknown	Unknown	32	13	0.41	Brain	CR: 55:5213
12-11.2	.0175121	17		0.18	Brain	CR 50:5784
Unknown	D17S5:28-31	14	0	0	Brain	AUR 145;11
Unknown	D17S5:28-31	25	6		Brain	CGC 73:122
Unknown	D17S5:28-31	15	5	0.33	Brain	CGC 73(122
Unknown	D17966	15				CGC 73:122
13.3	Unknown	28	10	0.36	Brain-	AJP 145,11
13	Unknown	51	17	0.33	Breast	HMG 4:2047
13.3	Unknown	27	16	0.59	Breast	÷ Lan 336:76
13,3	Unknown	22	9	0.41	Breast	HMG 4:2047
13.1-13.3	Unknown	88	38	0.43	Breast	HMG 4:2047
13.1	Unknown	16	6	The state of the s	Breast	CR 51:5794
13.3	Unknown	21	7	0.33	Breast	CR 53:1617
13.3	D1791174	7	3	**************************************	Breast	HMG 4:2047
13	D17S513	17	6	0.43	Breast:	HMG 4:2047
Unknown	D17566	7	7	0.35	Breast	CR 53:2947
13	Unknown	15	0	1	Breaur	CR 54:4200
13.3	Unknown	1.0		0	Cervix	BJC 67:71
13.3	Unknown	3	3		Colon	S:April 36
-13:3	Unknown	1	3	1	Colon	S:April 16
13.3	Unknown	4		1	Colon	SYADILL 126
		7	4	1	Colon	S:April 16

Chromosome 17 - p Arm

13.1	Unknown		2	To the second	Collons	Sciencesap
Unknown	HF-12					1980 7
		12	6	0.5	Colon	JNCI 84:11
13			20	0-62	Leophagea	0.00
	D17S513	32	20	0.62	Head&Neck	C 73:2472
13.2	CI17-732	The second second	5	-0275		Control of
Y-100	# DI 1984 : DI 5979 6	35	1	0.03	Kidnev	BJC 69:230
Unknown	D175849-D175796			0	Kidney	37N0C CV.578
Unknown-	D1797786-799	21	1	0.05	Kidney	PNAS 92:28
Unknown	Unknown		4	0.00	SEAUX mires	CRASSISSIN
13	Unknown	30 19	28	0.93	Lung	CR 54:2322
Unknown	D17S1-D17S28		10	0,53	Ovary .	
10.1	D1791-017528	15	2	0.13	Ovary	IJC 54:546
13.1-13.3	D17S34-D17S28-	7	10	0.18	107717777	1000
	D17S5-D17S379-	,	7	1	Ovary	AJHG 55:66
	P53-D17S513					
13.1-13.3		2.3	2 2			
	D1785-D178379-				Ovary	AJHGYAS 66
13.1-13.3	P53-0178513 D17834-D17828-					444
	D17S34-D17S28- D17S5-D17S379-	12	12	1	Ovary	AJHG 55:66
***************************************	P53-D17S513					
13.1-13.3	D17934-D17928-	1	1	1		
	D1785-D178379-			1	Ovary	AJHG 55:66
Unknown	P53-D178513				43 P. P. S.	
Unknown	D17S5-34-71- MYH2	36	29	0.81	Ovary	CR 53:2393
13	D179513					C. 55.255
13.3	D175578	36	16	0.44	Ovary	CR 561606
13.3	D175576	29	12	0.41	Ovary	CR 56:606
13.3	D17S695	27	17	0.63	Ovary	CR 56:606
Unknown	D175:34-5-28-31	41 19	18	0.44	Ovary	CR 56:606
Unknown	TP53-D17S:515-	18	12	0.63	Ovary	CGC 85:43
	520-513	10	9	0.5	Ovary	BJC 72:133
Unknown	D1791-D17528	7	Ō	0		
12.0-13	D17S1149	15	4	0.27	Prostate	G 11:530
Unknown	D1751-D17528	8	2	0.27	Prostate	GCC 13:278
Unknown	Unknown	19	2	0.11	Stomach,	GCC 37468
Onknown	D179134	17	0	0.11	Testis	G 5:134
Unknown	D17S30-D17S787	24	2	0.08	Testis	GCC_13:249
Unknown	1266	22	2	0.08	Testis	LI 73:606
SUM		10343	4539	0.44	Uterus	CR 54:4294
			·	0.77		

Chromosome 17 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	D	_
Onknown	2. 10 Page 18 for			The second secon	Tumor Type Ovary	Reference
11.2-12	D17S33	8	1	0.12		AIUC 54.276
11.2-12	0177-351	9		0.12	Brain	CR 49:6572
11.2-12	D17S33	59	13	0.22		CP-097(657/2074
11.2-12	er folgi er i K risch	Section Section		-0.22	Breast	CR 51:5794
11.2-12	D17533	7	2	0.29	Comment of the	(0) 53#4V31.7/2#
11.2-12	all filtress	Control of the state of the sta		0.23	Sarcoma Sarcoma	CR 52:2419
11.2-12	CRYB1	13	0	0	Brain	а.н.с;(риз <i>т</i> т, з
11.2-12	0.47	28		2002 TO V		AJP 145:1175
11.2-12	CRYB1	16	٥	0	Ereast Colon	GCC 4:115
Unknown	0176117			G.4		JNCI 84:1100
Unknown	D17573	25	6	0.24		CR 53:5517//
(CEN-172				0.24	Breast	0 8:781
CEN-12	D17S73	7	3	0.43	Breast	ECC 54.651617.018
	DESCRE	100			Ovary	IJC 54:85
11.2-12	THRA1	37	10	0.27	Breast	erecent stage)
11.2-12	THRAI	66		0.26		CR 54:2549
11.2-12	THRA1	14	11	0.79	Breast	GGC 10050
11,2-12	THRA1	17		0.41	***************	CR 52:2624
11.2-12	THRA1	13	5	0.38	***************************************	AJOG 172:908
11,2-12	THRAI	17	17	.0.71	Esophageal Ovary	CL 97:129
11.2-12	THRA1	20	1	0.05	Ovary	AJOG 172:908
13.1	TCF2	26	7	0.03	Read&Neck	IJC 54:220
21.1	RARA	11	6	0.55	Ovary	0.9:2077
11.2-12	D178256	1	0	0.33	Bladder	IJC 54:85
21	D17S250	5	1	0.2	Breast	HG 94:231
21	D17S250	81	17	0.21	Breast	CR 54:6069 CR 54:2549
21	D17S250	78	18	0.23	Breast	GCC 11:58
11.2-12	0178250	26	5	0.19	Breast	O 8:781
11.2-12	D17S250	6	1	0.17	Breast	HG 94:231
11.2-12	D17S250	14	7	0.5	Breast	CR 52:2624
21	D17S250	11	2	0.18	Esophageal	CL 97:129
11.2-12	D175250	19	5	******************************	Head&Neck	CR 54:1152
11.2-12	D17S250	2	0	0	Ovary	HG 94:231
11.2-12	D175250	22	14	0.64	CONTRACTOR OF THE PROPERTY OF THE PARTY OF T	BJC 69: 429
11.2-12	D17S250	20	2	0.1	Prostate	0 11:1241
21	D175250	20	2	0.1	Prostate	CR 55:1002
21	PHB	4	3	0.75	Ovary	IJC 54:85
Unknown	рив	9	9	1	Ovary	IJC 54:220
21	D175800	1	0	0	Bladder	HG 94:231
21	D178800	7	6	0.86	Breast, ·	CR 54:6069
21	D17S800	4	0	0	Breast	HG 94:231
21	D17S902	37	10	0.27	Breast	CR:54:2549
21	D17S902	16	4	0.25	Prostate	GCC 13:278
21	D178579	1	0	0	Bladder	HG1942231
21	D17S579	19	11	0.58	Breast	CR 52:2624
				·		56.2021

Chromosome 17 - q Arm

21	D178979	-				
21	D17S579	34	2	0.71		and the state of
21	DITESTO		20	0.21	Breast	0 8:781
21	D17S579	16	5		Breast	GCC NOST
21	01/79570	976		0.31	Breast	AJOG 172:908
21	D17S579	4	1	0.25	Breast	CR 54:2549.8
21	0146570	S 572		0.25	Breast	HG 94:231
21	D17S579	14	4	0.29	Dreast :	A BCRT 3/2 SO
21	D178579	26 =	8	0.29	Esophageal	CL 97:129
21	D17S579	17	1.3	0.76	"Read&Neck Ovarv	
21	0178579	23	9	***************************************	Cvary	AJOG 172:908
21	D17S579	2	0	0	Ovary	1.00
21	D178579	18	16	0.78	Ovary	HG 94:231
21	D17S579	37	22	0.59	Ovary	CR 56:606
74	(1) (1)	100	ATT TO THE STATE OF		Ovally Ovally	CR 36:606
21	D17S579	20	2	0.1	Prostate	CR 55:1002
21	0), 19579	200	97, 177		Programa	
21	D17S579	25	0	0	Uterus	CR 54:4294
Onkoown	D175509-	75	18	0.243	Breast	CR 53:4356
Unknown	D17S509	26	3	0.12	Breast	HG 91:6
Unknown	D175509	-11	2.5	0.45	Liver	CR 51:89
21	HOX2	19	1	0.05	Prostate	0 11:1241
Unknown	PPY	20	5	0.25	Breast	CR 53:5617
Unknown	D175806	26	2	0.08	Cervix	CR 56:197
21.3-22 22	COLLAI	24-	-10	0.42	Breast	0.8:781
12:0-24	D17S41	43	21	0.49	Breast	CR 53:5617
22	D17541	20	9	0.4	Breast	O.8:781
12:0-24	D17S41	11	7	0.64	Ovary	IJC 54:85
12.0-24	D17541 D17541	20	. 5	0.25	Ovary	IJC 54:546
21.3-22	NM23	8	7	0.88	Ovary	IJC 54:220
21.3-22	NM23	23	-G	0.26	Breast	GCC 4:113
71.3-22	NM23	61 29	8 3	0.13	Breast	ANYAS p.137
21.3-22	NM23	17		0.0	Colon	CR.54:3979
21.3-22	NM23	7	3 0	0.18	Colon	EJC 30A:664
21.3-22	NM23	20	13	0	Melanoma	GCC_7:169
21.3-22	NM23	23	13 2	0.65	Ovary	IJC 54:85
21.3-22	NM2 3	7	. <u>∠</u> 0	0.09	Stomach	JJCR 84:184
Unknown	NME 1	55	25	0	Uterus	C 73:1686
Unknown	NME1	6B	20	0:45	Breast	CR_53:5617
Unknown	NME1	17	. 5	0.29	Breast	GCC 11:58
Unknown	NME1	45	10	• 0:29	Breast	CR::52:2624
Onknown	NME1	48	7	0.22 0.15	Breast	BCRT 28:231
Unknown	NME1	18	1	0.06	Breast	JUCR 84:1159
Unknown	NME1		2	0.06	Cervix	CR 54:4481
Unknown	NME1	27	2	0.07	Escphageal: Head&Neck	
		*	-	0.07	neadaneck	C 73:2472

Chromosome 17 - q Arm

Unknown	Silvaria de la companya de la companya de la companya de la companya de la companya de la companya de la compa	A P. Ye				
Unknown	NME1	21	1			File ClayDing
Unknown	SWEET		1	0.05	Prostate	JU 151:1073
Unknown	NME1	18	8			NO 45/2/5
Unknown	N. O. S. C.		•	0.44	Testis	0 9:2245
22	D17574	50	10			Section of the section of
22-	OF COURT		10	0.2	Breast	BCRT 28:231
22	D17574	67	13		Televice .	eduli uz politika ili
Unknown	Gyryriy .	292	13	0.19	Breast	HG 91:6
22	D17S74	106	49	0.00		and some state of
Onknown	DIESTA	100	49	0.46	Breast	CR 54:4200
23	D17S74	49	12		a ince	AND CHAPTER
(University)			12	0.24	Breast	CR 53:3382
Unknown	D17574	57				
A 121 11 11 11 11 11 11 11 11 11 11 11 11	A	37	10	0.18	Breast	JJCR 84:1159
Unknown	D17S74	54	20			4:E-3: (G.)
Section of the second	Carrie Carrie Carrie		Witness and the second second	0.37	Esophageal	GCC 10:177
Unknown	D17574	30	3			(A) (A) (A) (A)
Unkpown	D17976	20	3	0.1	Kidney	CR 51:820
Unknown	D17574	12	2		Liver	
22	D17574		2	0.17	Liver	CR 53:368
22	D17S74	9	8		Lung 3	CR 49:5100-
22	D17974	3000	5	0.89	Lung	PN 86:5099
22	D17S74	11		0.93**	Lung	PN 8515099
Unknown	017574	39*	2	0.18	Lung	PN 86:5099
Unknown	D17S74	24	10	0,21	Lung	CR-52-2478
Unknown	D17574	23	16	0.42	Ovary	IJC 54:546
Unknown	D17574	26	10	0.77	Cyary	100 50 270
23	D17574	6	10	0.38	Ovary	CR 51:5118
23	D17574	8	1	0 10	Cverv	CR 53:3382
22	017574	10	2	0.12 0 .2	Ovary	CR 53:3382
23	D17S74	17	6	0.35	_Ovary	IJC 52:575
23	D17574	10	2	0.33	Ovary	CR 53:3382
22	D17S74	17	12	0.71	Cvary.	CR:53;3382
Diknown	D17974	18	49	0.71	Ovary	IJC 54:85
Unknown	D17S74	22	3	0.14	Sarcoma :	CR 4926247
Unknown	MPÓ	11	4	0.14	Sarcoma	CR 52:2419
Unknown	MPO	31	5	0.16	Breast:	CR_52:2624
Doknowa	ИРО	20	3	0.16	Head&Neck	0 9:2077
Unknown	D17S86	4 4	9	0.2	Prostate	
21.1-21.2	CI17-24	36	13	0.2	Breast	CR 53:5617
12-21.1	C117-316	37	11	0.3		CR_54 1638
12-21-1	C117+316		9	0.28	Breast	CR 53:3382
12-21.1	C117-316	13	6	0.46		CR:54:1638_21
17-21.1	C1117-316		0	0.46	Ovary	CR 53:3382
12-21.1	C117-316	9	1	0.11	Ovario	
		-	•	0.11	Ovary	CR 53:3382

Chromosome 17 - q Arm

12-21:1	C117-316	3	0	0	Overy	CR 53:3382
21.3	CI17-477	32	22	0.69	Esophageal	CR 54:1638
21.3	CI17-28	7	7 3	0.43	Esophageal	CR 54:1638
21.3	CI17-28	26	15	0.58	Esophageal	CR 54:1638
21,3	C117-592	18	8	0.44	Breast "	CR:53:3382
21.3	C117-592	17	6	0.35	Esophageal	CR 54:1638
21.3	C117-592	4	2	0.5	Ovary	CR 53:3382
21.3	C117-592	1	0	0	Ovary	CR 53:3382
21,3	C117-592	3	2	0.67	Ovary	CR 53:3382
21.3	C117-592	1	0	0	Ovarv	CR 53:3382
21.3	C117-701	138	48	0.35	Breast	-CR 53:3382
21.3	C117-701	38	21	0.55	Esophageal	CR 54:1638
21,3	C117-701	12	5	0.42	Overy	CR 53:3382 =
21.3	C117-701	7	0	0	Ovarv	CR 53:3382
21.3	C117-701	15	9	0.6	Ovary	CR 53:3382
21.3	C117-701	12	2	0.17	Ovarv	CR 53:3382
21.3	C117=730	96	36	0.38	Breast	CR 53:3382
21.3	C117-730	35	20	0.57	Esophageal	CR 54:1638
21.3	C117-730	4	0	0	Ovary	CR 53:3382
21.3	C117-730	4	0	0	Ovary	CR 53:3382
21,3	C117-730	12	6	0.5	Ovary	CR 53:3382
21.3	C117-730	4	2	0.5	Ovary	CR 53:3382
21.3	C117-507	25	7	0.28	Breast	CR 53:3382
21.3	C117-507	18	10	0.56	Esophageal	CR 54:1638
21.3	C117-507	3	1	0.33	Ovary	CR 53:3382
21.3	C117-507	5	2	0.4	Ovary	CR 53:3382
21.3	C117-507	7	6	0.86	Ovary	CR 53:3382
21.3	C117-507	3	1	0.33	Ovary	CR 53:3382
21.3	C117-533	93	25	0.27	Breast	CR 53:3382
21.3	C117-533	42	21	0.5	Esophageal	CR 54:1638
21.3	C117-533	9	4	0,44	Ovary	CR 53:3382
21.3	C117-533	9	3	0.33	Ovary	CR 53:3382
21,3	C117-533	11	6	0.55	Ovary	CR 53:3382
21.3	C117-533	7	1	0.14	Ovary	CR 53:3382
21-23	D17S78	14	0	. 0	Brain	AJP 145:1175
21-23	D17S78	25	5	0.2	Ovary	IJC 54:546
22-24	GH	39	13	0.33	Breast	0.8:761
22-24	GH	16	4	0.25	Breast	CR 52:2624
22-24	GH	59	iβ	0.22	Breast	CR 53:5617
22-24	GH	12	1	0.08	Lung	CR 49:5130
22-24	GH	14	7	0.5	Ovary	G0155:245
22-24	GH	15	1	0.07	Uterus	CR 51:5632
Unknown	46.E6	11	4	0.36	Breast	O 8:781
23-24	D17540	23	10	0.43	Breast	CR 53:5617
Unknown	D17S4D	14	5	0.36	Breast;	0 8:781
23-24	D17\$40	15	9	0.6	Ovary	IJC 54:85

Chromosome 17 - q Arm

Unknown	D17540	18-	4	0.22	Ovary	IJC 54:546 %
23-gter	D17S21	15	0	0	Brain	AJP 145:1175
23-qter	D17S21	20	7: ***	0.35	Breast	CR 53:5617
23-qter	D17S21	25	13	0.52	Ovary	IJC 54:546
Unknown	D17S515	32	6	0.19	Read&Neck	0 9:2077
Unknown	D17S801	32	4	0.12	Cervix	CR 56:197
Onknown	D178785	37	1	0.03	Head&Neck	CR 54:4756
Unknown	D175785	37	16	0.43	Head&Neck	CR 54:4756
Unknown	D17S785	-6	3	0:5	Kidney	GCC 12:76
Unknown	D17S785	27	1	0.04	Melanoma	CR 56:589
Unknown	CACNLB1	19 🗸	2	0.11	Prostate	0 11:1241
Unknown	D17S20	72	5	0.07	Breast	CR 53:5617
23-25,5	D1794	9	- 0	0	Brain	CR 49:6572
23-25.5	D17S4	14	3	0.21	Brain	CR 49:6572
23-25.5	D1754	34	1	0.03	Brain	AJP 1145-1175
23-25.5	D17S4	47	6	0.13	Breast	HG 91:6
23-25.4	D1794	42	18	0,43	Breast	BJC=69:754
23-25.3	D17S4	51	21	0.41	Breast	CR 54:4200
23-25.3	D1754	34	10	0.29	Breast	IJC 53:11
23-25.3	D17S4	104	28	0.27	Breast	CR 51:5794
23-25.3	D1754	63	24	0.38	Breast	CR 53:5617
23-25.3	D17S4	34	10	0.29	Breast	GCC 4:113
23-25.5	D1754	47	16	0.34	Breast	Lan 336:761
23-25.3	D1754	36	7	0.19	Breast	ANYAS p.137
23-25.5	D1754	35-	3	0.09	Cervix	CR 54:4481
23-25	D1754	13	0	0	Cervix	BJC 67:71
23-25.3	D1754	20	3	0.15	Colon	JNCI 84:1100
23-25.3	D1754	23	0	0	Colon	CCG 48:167
23-25.5	D1754	25	5	0.2	Colon	CR 50:7166
23-25.5	D17S4	14	1	0.07	Esophageal	CR 51:2113
23-25.3	D1754	23	7	0.3	Esophageal	CR 54:2996
23-25.5	D17S4	14	1	0.07	Kidney	CR 51:1071
23-25.5	D1754	8	2	0.25	Liver	CR 53:368
23-25.3	D1754	5	0	0	Liver	PNAS 86:8852
23-25.3	D1754	. 2	0	, <u>Q</u>	Lung	CR 49:5130
23-25.3	D17S4	16	11	0.69	Ovary	0 7:2069
23-25.3	D1754	16	2	0.12	Overy	0 7:2069
23-25.3	D17S4	41	30	0.73	Ovary	0 7:2069
23-25.3	D1764	2.2	4	0.57	Ovary	Unknown
23-25.3	D17S4	29	11	0.38	Ovary	IJC 54:546
23-25.3	D1756	21	2	0.1	Ovary	CR 51:5118
23-25.3	D17S4	30	11	0.37	Ovary	IJC 52:575
23-25	D1754	15	. 10	0,67	Ovary	TJC 54:85
23-25.5	D17S4	15	10	0.67	Ovary	IJC 54:85
23-25.3	D1754	19	12	0.63	Ovary	IJC 54:220
23-25	D17S4	4	С	0	Pancreas	CR 54:2761

Chromosome 17 - q Arm

23-25	D1794		0			
23-25	D17S4	9	2	0	Prostate	GCC 11:119
23-25.5	D1754	12		0.22	Sarcoma	CR 52:2419
23-25.3	D1754	14	9 3	0.75	Sarcoma	CR 52:2419
23-25	D1794	7	0	0.21	Sarcoma	CR 49:6247
23-25.5	D1754	42		0	Stomach	CR 51:2926
23:3-25.3	TKI	21	17	0.4	Testis	0 9:2245
23-ater	D17877	31		0.05	Breast	CR 53:5617
23-qter	D17577	30	2 11	0.06	Brain	AJP 145:1175
Unknown	D17526	9	0	0.37	Breast	CR 53:5617%
Unknown	D17526	16	5	0	Breast	CR 53:5617
23-25	D17526	***************************************	***************************************	0.31	Ovary	CR 50:2724:
23-25.3	D17575	71 23	23	0.32	Breast	CR 51:5794
Unknown	D17524		0	0	Brain	AJP 145:1175
Unknown	D17524		12	0.35	Breast	GCC 4:113
Unknown	D17S24	59 59	27	0.46	Breast	CR 53:5617
23-25.3	D17524		20	0.34	Breast	0 8:781
23-25	D17824	40	17	0.42	Breast	CR 54:4200°
23-25.3	D17524	4.2 4.0	10	0.24	Breast	CR 51:5794
23-25.3	D17524	**********	17	0.42	Breast	CR 54:4200
23-25.3	D17524	20	8	0.4	Breast	GCC 2:191
Unknown	D1/824	******************	2	0.5	Breast	CR 53:3804
23-25.3	MAIN PROSTORES CONTRACTOR CONTRAC	21	2	0.1	Colon	JNCI 84:1100
Unknown	D17524	. 18	11	0.61	Ovary	IJC 54:85
23-25.3	D17S24	16	8	0.5	Ovary	IJC 54:546
23-25	D17S24	18	11	0.61	Ovary	IJC 54:85
Onknown	D17S24	3	0	0	Ovary	CR 51:5118
23-25	D17S24	9	1	0.11	Prostate	G 11:530
Unknown	D17527	17	6	0.35	Breast	CR 51:5794
Unknown	D17579	. 9	2	0.22	Breast	CR 53:5617
Unknown	D17579	9	2	0.22	Breast	CR 53:5617
12.0-21	D17S588	1	<u> </u>	0.	Bladder	HG 94:231
Unknown	Unknown	1 28	0	0	Bladder	HG 94:231
25.1	Unknown	46 31	3 .	0.11	Brain	CR 50:5784
23	Unknown	31	10	0.29	Breast	CR 53:3382
22	Unknown	41	*************************************	0,32	Breast	CR 53:3382
25.3	Unknown	45	14	0.34	Breast	CR 53:3382
21	D173700	5 4	***************************************	0.29	Breast	CR 53:3382
21	D1751184	11	10 2	0.19	Breast	CR 54:2549
21	D17S1322	11		0.18	Breast	CR 54:6069
21	D1751325	. 11	11	0.91	Breast	CR 54:6069
21	D1751328	6	<u>11</u> 5	1	Breast	CR 54:6069
21	D175183	36	5 6	0.83	Breast	CR 54:6069
Unknown	D1752		0	0.22	Breast	CR 54:2549
Unknown	D175293	15	3	0	Breast	GCC 2:191
Unknown	D17S308	23	9	, 0.2	Breast	AJOG: 172:908
	01/3300	43	7	0.39	Breast	0 8:781

Chromosome 17 - q Arm

Unknown	D1795-D1781- D17931-D178509-	75	18	0.24	Breast	CR 53:3707
	D17974-D1794					
Unknown	D17S587	6	1	0.17	Breast	HG 94:231
12.0-21	D178588	9	2 *	0.22	Breast	0 8:781
12.0-21	D175588	6	1	0.17	Breast	HG 94:231
12.0-21	D17S588	17	8	0.47	Breast	AJOG 172:908
21	D17S648	39	7	0.18	Breast	CR 54:2549
Unknown	D17568	23	16	0.7	Breast	CR 54:4200
21	D17S702	92	21	0.23	Breast	CR 54:2549
Unknown	D175702	80	24	0.3	Breast	GCC 11:58
Unknown	D17S733	65	18	0.28	Breast	GCC 11:58
21	<u>D175746</u>	36	10	0.28	Breast	CR 54:2549
21	D17S750	59	14	0.24	Breast	CR 54:2549
23-qter	D17577	_30_	11	0.37	Breast	CR 53:5617
Unknown	D175773	9	2	0.22	Breast	CR 53:5617
21 21	D175776	10	6	0.6	Breast	CR 54:6069
21	D17S776	70	17	0.24	Breast	GCC 11:58
21	D175776	63	19	0.3	Breast	CR 54:2549
21	D175846 D175855	74	24	0.32	Breast	CR 54:2549
21	D178855	30	8	0.27	Breast	CR 54:2549
21	D175855	86	21 B	0.24	Breast	GCC 11:58
21	D17S856	10		0.8	Breast	CR 54:6069
21	D175857	53 68	10	0.19	Breast	CR 54:2549
21	D178859	17	17	0.25	Breast	CR 54:2549
21	D175870	441	2 173	0.12	Breast	CR 54:2549
21	D17S870-CI17-730	289	98	0.39	Breast	BJC 71:438
Onknown	EDH178-HSD-A3T	19	7	0.34 0.37	Breast	C 74:2281
Unknown	EDH17E-HSD-DEL	20	9	0.45	Breast	GCC 11:58
Unknown	EPB3	15	Ď.	0.4	Breast Breast	GCC 11:58 CR 53:5617
21	GAS	50	13	0.26	Breast	CR 54:2549
Unknown	PROHIB	6	1	0.17	Cervix	GCC 9:119
Unknown	D17S791	22	1	0.05	Endocrine	CR 56:599
25.3	Unknown	40	11	0.28	Esophageal	CR 54:1638
22	Unknown	33	16	0.48	Esophageal	CR 54:1638
25.1	Unknown	26	14	0.54	Esophageal	CR 54:1638
Unknown	D175874	35	20	0.57	Esophageal	GCC 10:177
Unknown	GP3A	15	6	0.4	Read&Neck	0 9:2077
12.0-21	D17S588	34	2	0.06	Kidney	BJC 69:230
Onknown	D175:802-805-809	22	5	0,23	Leukemia	CR 55:5377
Unknown	D17S32	13	0	0	Liver	CR 53:368
25.3	Unknown	7	3	0.43	Ovary	CR 53:3382
22	Unknown	3	1	0.33	Ovary	CR 53:3382
25.1	Unknown	7	0	0	Ovary	CR 53:3382
25.1	Unknown	17	6	0.35	Ovary	CR 53:3382
22	Unknown	3	0	0	Ovary	CR_53:3382

Chromosome 17 - q Arm

25.3	Unknown	8	3	0.38	Ovary	CR 53:3382
25.3	Unknown	8	(0.5	Ovary	CR 53:3382
22	Unknown	5	4	0.8	Ovary	CR 53:3382
25.3	Unknowa	6	0	0	Ovary	CR 53:3382
22	Unknown	1	0	0	Ovary	CR 53:3382
23	Unknown	3	0	0	Ovary	CR 53:3382
23	Unknown	5	5	1	Ovary	CR 53:3382
25.1	Unknown	11	6	0.55	Overy	CR 53:3382
25.1	Unknown	10	1	0.1	Ovary	CR 53:3382
23	Onknown	2	0	Q	Ovary	CR 53:3382
23	Unknown	8	3	0.38	Ovary	CR 53:3382
Un known	46E6-HOX2B-	18	10	0.56	Overy	BJC 72:1330
	D17S:250-588-579					
Unknown	D17S136	6	5	0.83	Ovary	IJC 54:220
Unknown	D17S174	10	- 8	0,8	Overy	IJC 541220
Unknown	D17S180	6	4	0.67	Ovary	IJC 54:220
.Baknown	D17S250-579-588- NM23-GH	120	.64	0,53	. Ovary	CR.53;1218
12.0-21	D17S250-THRA1- D17S846-D17S856- D17S855-D17S183- D17S579-D17S588	3	2	0.67	Ovary	AJHG 55:666
12.0-21	D17S250-THRA1- D17S846-D17S856- D17S855-D17S183- D17S579-D17S588	14	12	0.86	Overy	AJHG \$5:666
12.0-21	D17S250-THRA1- D17S846-D17S856- D17S855-D17S183- D17S579-D17S588	11	8	0.73	Ovary	AJHG 55:666
12.0-21	D17S250-THRA1- D17S846-D17S856- D17S855-D17S183- D17S579-D17S586	1	1	1	Ovaty	AJHG 55:666
Unknown	D17S293	11	9	0.82	Ovary	IJC 54:220
Unknown	D17S293	18	14	0.78	Ovary	AJCG 172:908
Unknown	D175308	17	14	0.82	Ovary	IJC 54:220
Unknewn	D17S587	2	0	0	Ovary	HG 94:231
12.0-21	D17S588	11	6	0.55	Ovary	BJC 69:429
12.0-21	D17S588	20	14	0.7	Ovary	AJCG 172:908
12.0-21	D17S588	2	0	0	Ovary	HG 94:231
Unknown	D17S73-41-4-77	37	28	0.76	Overy	CR 53:2393
22-23	NME1-D17S74-GH- D17S40-D17S4- D17S75	11	11	1	Ovary	AJHG 55:666
22-23	NME1-D17S74-GA- D17S40-D17S4- D17S75	3	3	1	OVAEY	AJHG .55: 666

Chromosome 17 - q Arm

22-23	NME1-D17S74-GH- D17S40-D17S4- D17S75	1	1	1	Ovary	AJHG 55:666
22-23	NME1-D17S74-GH- D17S40-D17S4- D17S75	14	14	1	Cvary	AJHG 55:666
Unknown	D1751323	12	3	0.25	Prostate	0 11:1241
Unknown	01791327	15	2	0.13	Prostate	0.11:1241
12.0-21	D17S588	19	2	0.11	Prostate	CR 55:1002
12,0-21	D178588	19	2	0.11	Prostate	0 11:1241
21.3	D17S752	14	1	0.07	Prostate	GCC 13:278
21	D17S776	12	5	0.42	Prostate	0 11:1241
21	D17S846	19	2	0.11	Prostate	0 11:1241
21	0175855	18	8	0.44	Prostate	0 11:1241
21	D17S855	18	8	0.44	Prostate	CR 55:1002
21	D178856	15	5	0.33	Prostate	D 11:1241
21	D17S856	15	6	0.4	Prostate	CR 55:1002
21	D17S857	20	2	0.1	Prostate	0.11:1241
21	D17S859	18	1	0.06	Prostate	0 11:1241
Unknown	KPT 9	18	2	0.11	Prostate	O 11:1241
Unknown	D17532	10	1	0.1	Sarcoma	CR 49:6247
Unknown	D17S32	14	2	0.14	Sarcoma	CR 52:2419
Unknown	D17S293	19	0	0	Uterus	CR 54:4294
Unknown	PROHIB	2	1	0.5	Oterus	GCC 9:119
SUM		9605	3006	0.31		Commence on A. A. as bridge II History and L.

Chromosome 18 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
11.2-12.1	TTR	19	9	.0.5	Colon	LJC 53:382
11.1-11.2	D1857	5	2	0.4	Breast	CR 53:3804
11.1-11.2	D1857	77	- 22	0-29	Colon	
11.1-11.2	D1857	9	2	0.22	Stomach	HG 92:244
11,1-11.2	D1857	17	8	0:473	Stomach	CR:52:3099
Unknown	D18S1	7	1	0.14	Breast	GCC 2:191
Unknown	D1891	8		0.5	Colon	IJC 53:382
Unknown	D1851	11	0	0	Colon	
Unknown	D1851	16	4	0.25	Colon	N 331:273
Unknown	D18S1	1	1	1	***************************************	CR:50:7166
Unknown	D1891	5	7		Lung	PNAS 86:5099
Unknown	D18S1	4	1	0.4	Lung	PNAS_86:5099
Unknown	D18S1	9	1	0.25	Lung	PNAS 86:5099
Unknown	D18S1	15		0.33	Ovary	0.7:1059- K
Dnknown		**************************************	7	0.47	Sarcoma	CR 52:2419
	D1891	- 6	2	0.33***	elikaan k	CR/51:5632
11	D1856	8	2	0.25	Bladder	BJC 70:697
11	D1856	12	- 2	0.17	Exeast	PRAS 87.7737
ll-pter	D1856	24	5	0.21	Breast	JNCI 84:506
11	D1896	16	. 6	0,38	Cervix	CR 54:4481
11	D18S6	19	9	0.47	Colon	CR 50:7166
11	D1856	6	0	0	Calán	CCG 48:167
11	D1856	17	3	0.18	Ovary	IJC 54:546
11	D1856	1	0	0.	Prostate	JU 151:1073
11	D18S6	15	4	0.27	Testis	0 9:2245
11	D1856	5	1	0.2	Testis	GCC 13:249
Unknown	D18S57	33	10	0.3	Cervix	CR 56:197
Unknown	D18522	14	2	0.14	Brain	CR 50:5784
Unknown	D18S22	17	3	0.18	Breast	GCC 2:191
Unknown	D18922	29	11	0.38	Esophageal	CR 54:2996
Unknown	D18S22	11	7	0.64	Sarcoma	CR 52:2419
21,3	D1898	7		0.43		CR 53:3804
21.3	D18S8	27	9	0.33	Colon	S 241:961
21.3	D1858	7	5	0:71	Stomach	CR 52:3099
21.3	D1858	14	6	0.43	Stomach	HG 92:244
Unknown	D18524	13	1	0.08	Breast	CR 50:7184
Unknown	D18S24	6	0	0	***************************************	······································
Unknown	D18924	4	0	0	Cervix	GCC 9:119
Unknown	D18524	17			<u>Kidney</u>	CR.51:820
Unknown	D18524	8	4 0	0.24	Lung	CR 52:2478
Unknown	D18S24	~~ ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		0	Ovary	CR-51:5118
11.2-12.1	PALB	3	0	С	Uterus	GCC 9:119
11.2-12.1	****	18	9:	0.5	Colon	CR 50:7166
(CT:T070000000000000000000000000000000000	PALB	11	2	0.18	Colon	GCC 3:468
11.2-12.1	PALE	6	O	. 0	Pancreas	GCC 3:468 -4
11.2-12.1	PALB	8	2	0.25	Stomach	GCC 3:468
1112-12.1	PALB	3	0	0	Oterus	CR_51:5632
21.3	DCC	28	8	0.29	Bladder	CR 55:5213

Chromosome 18 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
11.21-PTER	018540	25		10.02	Oterus	CR-54:4294
Unknown	Unknown	12	1	0.08	Brain	CR 50:5784
Unknown	D18516	27	0	- 0	Ereast	ER 53:4356
11.3	D1853	9	1	0.11	Breast	CR 50:7184
Unknown	D18953.	31	8	0.26	Cervin	CR 56: 197
Unknown	D18S59	20	1	0.05	Endocrine	CR 56:599
Unknown	D18921	20,	2	0.2	Esophageal	CR:54:2996
Unknown	D18S21	15	1	0.07	Esophageal	CR 51:2113
Unknown	D18S3	10	2	0.00	Esophageal	The state of the s
11.21-PTER	D18540	22	6	0.27	Head&Neck	CR 54:1152
Unknown	D18S59	73	0	0	ReadsNeck	CR 54:4756
Unknown	D18S59	18	3	0.17	Head&Neck	CR 54:4756
11.3	D1853	112	0	0	Kidney	CR 51:820
Unknown	D18S59	21	0	0	Kidnev	PNAS 92:2854
Unknown	D18S59	6		0.17	Kidnev	PNAS 92 2854
Unknown	D18S54	19	1	0.05	Leukemia	CR 55:5377
321113	D1853	16		0.25	Lung	CR: 52: 2478
Unknown	D18S59	33	4	0.12	Melanoma	CR 56:589
11.3	D1853	- 6	0	0	Ovary	CR:51:5118
11.21-PTER	D18540	15	4	0.27	Ovary	BJC 72:1330
Unknown	D1856	10		0.1	Ovary	CR 53:2393
11.3	D1853	. 15	0	0	Prostate	G 11:530
Unknown	D18521	10	2	0.2	. Sarcoma	CR 52:2419
11.21-PTER	D18540	25	3	0.12	Uterus	CR 54:4294
SUM		388	45	0.12		

Chromosome 18 - q Arm

21.3	DCC	15			Bladder	BJC 70:697
21.3	DCC	26	2	0.08	Breast	CR 53:4356
21.3	DCC	16	5	0.31	Breast	BJC 68:64
21	DCC	5	1	0.2	Cervix	BJC 67:71
21.3	DCC	12	3	0.25	Cervix	BJC 67:71
21.3	DCC	48	18	0.38	Colon	EJC 30A:664
21.3	DCC	25	13	0.52	Colon	CR:54:3979
21.3	DCC	4	1	0.25	Colon	0 9:991
21.3	DCC	41	29	0:71	Colon	S 247:49
21.3	DCC	19	0	0	Endocrine	GCC 13:9
21.3	DCC	44	10	0.23	Esophageal	CR 54:3007
21.3	DCC	50	12	0.24	Esophageal	CR 52:6525
21.3	DCC	. 5	1	0.2	Kidney	GCC 12:76
21.3	DCC	19	11	0.58	Leukemia	B 83:3449
21.3	DCC	26	. 8	0.31	Leukemia	B 82:927
21.3	DCC	9	3	0.33	Leukemia	B 82:927
21.3	DCC	11	. 1	0.09	Liver	CR 91:89
21.3	DCC	6	2	0.33	Ovary	BJC 71:462
21.3	DCC	34	15	0.44	Ovary	0 7:1059
21.3	DCC	7	3	0.43	Ovary	0 7:1059
21.3	DCC	2	2	1	Pancreas	CR 54:2761
21	DCC	12	2	0.17	Prostate	PNAS 87:8751
21.3	DCC	11	5	0.45	Prostate	CR 53:2723
21.3	DCC	13	5	0.38	Prostate	GCC 11:119
21.3	DCC	12	2	0.17	Prostate	CSurveys 11:1
21	DCC	7	5	0.71	Stomach	CR 52:3099
21.3	DCC	18	5	0.28	Stomach	LI 74:835
21.3	DCC	10	5	0.5	Stomach	CR 52:3099
21.3	DCC	51	17	0.33	Uterus	CR 54:4294
21.3	DCC	8	1	0.12	Uterus	CR 51:5632
21.3	DCC	5	i i	0.2	Uterus	CR 51:5633
21.2-21.3	D18535	22	0	0	Uterus	CR 54:4294
21.3	BCL2	14	1	0.07	Breast	PNAS: 87:7737
21.3	BCL2	10	6	0.6	Colon	JJCR 85:584
21:3	BCL2	20	10	0.5	Ovary	0 7:1059
21.3	BCL2	7	2	0.29	Prostate	GCC 11:119
21.3	BCL2	17	4	0.24	Stomach	JJCR 85%584
Unknown	D18S68	23	8	0.35	Cervix	CR 56:197
Unknown	D18919	22	o" ,	0.41	Breast	PNAS 8727737
Unknown	D18S19	8	3	0.38	Prostate	GCC 11:119
21.3-qter	D1855 -	9	4	0.44	Bladder	BJC 70:697
12	D1855	17	4	0.24	Bladder	CR 51:5405
21.3-qter	D1855	.70	11	0.16	Breast	JJCR 8471159
12	D18S5	5	1	0.2	Breast	GCC 2:191
21.3-qter	D1855	43	6	0.14	Breast	AJP 140:215
21.3-qter	D1855	16	11	0.69	Breast	PNAS 87:7737

Chromosome 18 - q Arm

21.3-qter	D1895	21	2	0.1	Cervix	CR 54:4481
12	D18S5	7	0	0	Cervix	CR 49:3598
21.3-qter		6	2 *	0.33	Colon	0 9:991
21.3-qter	D18S5	21	16	0.76	Colon	IJC 53:382
12	D1895	19	12	0.63	Colon	CR 50:7166~
12	D18S5	29	11	0.38	Esophageal	GCC 10:177
12	DIES5	19	1	0.05	Kidney	CR 51:1544
12	D18S5	18	1	0.06	Liver	JJCR 81:108
12	D1835	28	3	0.11	Lung	PN 84:9252
12	D18S5	7	0	0	Neuroblaston	
					a	
21:3-qter	D1855	16	4	0.25	Ovarv	IJC 54:546
21.3-gter	D1855	15	9	0.6	Ovary	0 7:1059
21.3-qter	D1855	21	12	0.57	Prostate	JU 151:1073
21.3-qter	D18S5	16	4	0.25	Prostate	GCC 11:119
12	D1895	13	0.	0	Stomach	CR 48:2988
21.3-gter	D18S5	15	10	0.67	Stomach	CR 52:3099
21.3-qter	D1855	14	1	0:07	Testia	GCC 13:249
12	D18S5	4.2	16	0.38	Testis	0 9:2245
12	D1855	9	2	0.22	Uterus	CR 51:5632
Unknown	D18S58-D18S61	6	1	0.17	Kidnev	······································
Unknown	D18958-D18961	22	Ö	0.17		PNAS 92:2854
23	D18S11	67		······································	Kidney	PNAS 92:2854
23	D18311	8	17	0.25	Breast	PNAS 87:7737
	Annual Strategic Control of the Cont		3	0.38	Colon	GCC 3:468
23 23	D18511	25	8	0.32	Ovary	IJC 54:546
***************************************	D18911	35	21	0.6	Ovary	0 7:1059
23	D18S11	5	0	0	Pancreas	GCC 3:468
23	D18511	13	2	0.15	Prostate	GCC 11:119
23	D18S11	13	2	0.15	Stomach	GCC 3:468
Unknown	D18970	41	0	0	Read&Neck	CR 54:4756
Unknown	D18570	43	3	0.07	Head&Neck	CR 54:4756
Unknown	D18570	21	ō	Ö	Kidney	PNAS 92:2854
Unknown	D18570	6	1	0.17	Kidney	PNAS 92:2854
Unknown	D18570	23	5	0.22	Melanoma	CR 56:589
Unknown	D18S70	23	5	0.22	Melanoma	CR 56:589
12.1-21.1	Unknown	18	4	0.22	Bladder	BJC 70:697
23	Unknown	11	4	0.36	Bladder	BJC 70:697
Unknown	D18922	12	0	Ö	Brain	CR 49:6572
Unknown	D18S46	17	1	0.06	Endocrine	CR 56:599
Unknown	D18S34	26	6	0.23	BeadsNeck	CR 54:1152
Unknown	D18S:58-67	23	4	0.17	Leukemia	CR 55:5377
Unknown	Unknown	2	0	O	Liver	BJC 67:1007
Unknown	Unknown	5	0	0	Liver	BJC 64:1083
Unknown	DCC-D18S34	28	12	0.43	Ovary	CR 53:2393
Unknown	MBP- D18S:34-35	15	6	0.4	Ovary	BJC 72:1330
Unknown	PLANH2	7	2.	0.29	Ovary	0.7:1059
Unknown	Unknown	6	***************************************			~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
Oliviioali	CITATIOWIT	O	4	0.67	Pancreas	CR 54:2761

Chromosome 18 - q Arm

Unknown	Unknown	1	Ō	0	Pancreas	CR 54:2761
Unknown	Unknown	6	0	0	Pancreas	BJC 65:809
23	Unknown	2	2	1	Prostate	JU 151:1073
Unknown	D18S31	19	2	0.11	Testis	GCC 13:249
Unknown	JOSR4.4	20	5 -	0.25	Testis	0.9:2245
SUM		2301	659	0.29		

Chromosome 19 - p Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
Unknown	LIPE	21	0	0 - 0	Uterus	CR 54;4294
13.2-CEN	D19S11	36	2	0.06	Brain	AJP 145:1175
Unknown	D19520		.0	0	Brain	CR::50:5784
Unknown	D19S20	35	1	0.03	Brain	AJP 145:1175
Unknown	019920	8	0	. 0	Brain	CR: 49:6572
13.2	D19524	15	0	0	Brain	AJP 145:1175
12-13.2	D19576	14	0	- 0	Brain	CR 54:1397-
12-13.2	D19S76	11	1	0.09	Brain	CR 54:1397
13,7-13.1	LOLR	3	1 .	0.38	Brain	CR 54:1397
13.2-13.1	LDLR	11	0	0	Brain	CR 54:1397
13.2-CEN	D19511	26	7	0.27	Breast	CR 53:4356
Unknown	D19520	36	7	0.19	Breast	CR 50:7184
13.32	D19922,	35	1	0.03	Breast	CR 53:4356
13.2-CEN	D19S11	45	1	0.02	Cervix	CR 54:4481
13,3	D198177		4	0.15	Cervix	CR:56:197
Unknown	D19S20	8	0	0	Cervix	GCC 9:119
Unknown			7	0.24	Cervix	CR 56:197
Unknown	D19S7	26	4	0.15	Cervix	CR 54:4481
Unknown	D195216	22	I	0.05	Endocrine	CR 56:599
Unknown Unknown	D19S20	22	6	0.27	Esophageal	CR 54:2996
13.32	D19820	25	2	0.08	Esophageal	GCC 10:177
13.32.2	D19S22 D19S177	34	11	0.32	Esophageal	GCC 10:177
Unknown	D19S111	16	<u>4</u>	0.25	Head&Neck	CR 54:1152
Unknown	D195216	15 19	0	0	Head&Neck	CR 54:4756
Unknown	D19S221	19	1 6	0.05	Head&Neck	CR 54:4756
13.3	Unknown	48	7	0.32	Head&Neck	CR 54:1152
Unknown	D19S20	40	8	0:15	Kidney	CR 51:5817
Unknown	D19920	25	8	0.2 0.32	Kidney	CR 51:5817
13.3	D19S21	30	3	0.12	KiqueX	CR 51:820
Unknown	D195216	3	0	0.1	Kidney	CR 51:5817
Unknown	D195216	17	1	0.06	Kidney	PNAS 92:2854
13.2-TER	C3	3	0	0.00	Kidney	PNAS 92:2854
13.32	D19S22	28	1	0.04	Liver Liver	CCG 48:72
Unknown	D1987	11	0	0.04	Liver	CR 51:89 JJCR 81:108
Unknown	D19520	26	3	0.12	Lung	CR 52:2478
Unknown	D1957	17	0	0.12	Frind	PN 84:9252
Unknown	D195216	25	2	0.08	Melanoma	CR 56:589
Unknown	Unknown	19	5	0.26	Ovary	CR 51:5118
13.2-CEN	D19S11	16	3	0.19	Ovary	IJC 54:546
13:2-CEN	D19S11	13	2	0.15	Ovary	CR 53:2393
13.3	D19S177	11	5	0.45	Ovary	EJC 69:429
Unknown	D19\$20	13	5	0.38	Ovary	GO 55:198
Unknown	D19S20	24	8	0.33	Ovarv	CR 51:5118
13:3-13.2	INSR	21	5	0.24	Ovary	IJC 54:546
13.32	D19S22	6	0	0	Pancreas	CR 54:2761

Chromosome 19 - p Arm

13.2-CEN	D19S11	3	0	0	Prostate	G 11:530
Unknown	D19S20	21	5	0.24	Sarcoma	CR 52:2419
Unknown	D1957	3	1	0.33	Sarcoma	CR 52:2419
13.2-CEN	D19S11	46	2	0.04	Testis	0 9:2245
Unknown	D19820	20	1	0.05	Testis	LL 73:606
Unknown	D19S20	20	1	0.05	Testis	G 5:134
13,3-13.2	INSR	2	0	Ð	Testis	CCG: 52:72
13.3-13.2	INSR	3	0	0	Testis	CCG 52:72
13.3-13.2	Insr	1	0	0	Testis	CCG 52:72
Unknown	D19520	14	0	0	Uterus	GCC 9:119
Unknown	LIPE	21	0	0	Uterus	CR 54:4294
SUM		1099	143	0.13		

Chromosome 19 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
13.2	APOC2	:11	0	0	Uterus	CR 54:4294
13.2	APOC2	33	19	0.58	Brain	AJP 145:1175
13,2	APOC2	22	8	0.36	Brain :	CR 54:1397-
13.2	APOC2	15	1	0.07	Brain	CR 54:1397
13.1-13.2	BCL3	5	4	0:8	Brain	CR.54:1397
13.1-13.2	BCL3	6	1	0.17	Brain	CR 54:1397
13,3	CKMM	34	19	0.56		AJP 145:1175
13.2	CYP2	24	13	0.54	Brain	AJP 145:1175
13.2	D19S178	12	1	0.08	Brain	CR 54:1397
13.2	D19S178	18	5	0.28	Brain	CR 54:1397
13.4	D199180	21	9	0.43	Brain	CR 54:1397
13.4	D19S180	11	2	0.18	Brain	CR 54:1397
13.1	D195191	23	6 -	0.26	Brain	CR.54:1397
13.1	D19S191	12	2	0.17	Brain	CR 54:1397
13.4	D19522	18	1	0.06	Brain	CR 50:5784
13.4	D19S22	37	18	0.49	Brain	AJP 145:1175
12-13.1	D19930	15	7	0.47	Brain	AJP 145:1175
12-13.1	D19531	6	4	0.67	Brain.	AJP 145:1175
13.1	D19\$32	21	10	0.48	Brain	AJP 145:1175
13.1-13.2	D19S47	18	4	0.22	Brain	CR 54:1397
13.1-13.2	D19947	11	2	0.18	Brain	CR 54:1397
12-13.1	D19S49	22	5	0.23	Brain	CR 54:1397
12-13.1	D19S49	12	1	0.08	Brain	the state of the s
13.3	D19S51	12	7	0.58	Brain	CR 54:1397 AJP 145:1175
13.3	019862	12	7	0.58	Brain	
13.3	D19S63	24	15	0.62	Brain	AJP 145:1175
12	D1997	21	10	0.48	Brain	AJP 145:1175 AJP 145:1175
11-CEN	D19574	7	4	0.57	Brain	AJP 145:1175
12-13.1	D19975	11	***************************************	0.09	Brain	CR 54:1397
12-13.1	D19S75	19	3	0.16	Brain	CR 54:1397
13.2	D1998	21	14	0.67	Brain	AJP 145:1175
Unknown	D19S9	6	2	0.33	Brain	AJP 145:1175
13.3	ERCCL	32	18	0.56	Brain	A STATE OF THE PROPERTY OF THE PARTY OF THE
13.3	ERCC2	16	7	0.44	Brain	AJP 145:1175 1
13.2	APOC2	25	2	0.08	THE CONTRACTOR OF SAME PROPERTY OF SAME A	AJP 145:1175 GCC 2:191
13.4	D19S22	19	3	0.16	Breast	······································
13.2	APOC2	29	3	0.1	Breast	CR 50:7184
Unknown	D19S223	24	3	0.12	Cervix	CR 56:197
Unknown	D1989	1	o o	TOTAL COMPANY TOTAL CONTRACT OF THE PARTY OF	Cervix	CR 56:197
13.2	APOC2	17	1	0 0.06	Cervix	CR 49:3598
12	D1957	21	16	0.76	Colon	CCG 48:167
Unknown	D19S210	18	1		Colon	IJC 53:382
13.4	D19S22	23	7	0.06	Endocrine	CR 56:599
Unknown	D19S210	22	7	0.3	Esophageal	CR 54:2996;
Unknown	D19 5 255	10	0	0.32	Head&Neck	CR 54:1152
Unknown	D19S255	10	0	<u> </u>	Head&Neck	CR 54:4756
	0170200	10	U	0	Head&Neck	CR 54:4756

Chromosome 19 - q Arm

Unknown	D198210-D198224	6	0	Q	Kidney	PNAS 92:2854
Unknown	D195210-D195224	19	0	0	Kidney	PNAS 92:2854
13.4	D19922 ²	14	3	0.21	Kidney	CR 51:820
Unknown	D19S225	3	0	0	Kidney	PNAS 92:2854
Unknown	D199225	17	. 1	0.06	Kidney	PNA9 92:2854
13.4	D19S22	24	11	0.46	Lung	CR 52:2478
13.4	D19922	3	2	0.67	Lung	CR 52:2478
13.4	D19S22	1	1	1	Lung	CR 52:2478
13.4	D19522	9	9	1	Lung	CR 52:2478
Unknown	D195225	22	0	0	Melanoma	CR 56:589
12	D1987	3	Û	0	Neuroblasto a	om CR 49:1095
Unknown	CYPl	7	1	0.14	Ovary	CR 50:2724
13.4	D19922	16	A	0.25	Ovary	CR:51:5118
12-13.1	D19S49	13	3	0.23	Ovary	BJC 69:429
. 13.2	D1998	23.	- 5	0.22	Ovary	IUC:54:5461
Unknown	D19S8-CYP2A	23	4	0.17	Ovary	CR 53:2393
13.2	D1988	12	0	0	Prostate	G 11:530
13.4	D19S22	9	3	0.33	Sarcoma	CR 52:2419
12	D1957	16	1	0.06	Stomach	CR 48:2988
12	D19S7	19	2	0.11	Testis	0 9:2245
13.2	APOC2	11	0	0	Uterus	CR 54:4294
SUM		1066	323	0.3		

Chromosome 20 - p Arm

Band	Marker	Total	Cases with LOH	LOH Frequency	Tumor Type	Reference
12	D2056	4 ***		0.25	Uterus ***	CR: 51: 5632
Unknown	Unknown	12	1	0.08	Brain	CR 50:5784
12	D2056	9	0	0	Brain :	OR 49:6572
Unknown	D20S19	6	0	0	Breast	CR 53:3804
Unknown	D20819	37		0.05	alegisja – sa	CR 250 7184
12	D20S6	20	3	0.15	Breast	GCC 2:191
Unknown	0205118	31	0 -2	. 0	Cervix	CR: 56:197
Unknown	D20S19	3	0	0	Cervix	GCC 9:119
12	D20S6_	2	0	C	Carvix	CR 49 3598
12	D20S6	28	6	0.21	Cervix	CR 54:4481
Unknown	D20S98	16	2	0.12	Cervix -	CR 56:197
Unknown	D20S95	16	0	0	Endocrine	CR 56:599
Unknown	D20519	59	7.00	0.12		GCC 10 177
Unknown	D20572	20	2	0.1	Esophageal	CR 54:2996
Unknown	D209104	12	0	0	HeadsNeck	CR:54:4756
Unknown	D205104	23	2	0.09	Head&Neck	CR 54:4756
Unknown	D20595	20	. 6	0.3	.Read&Neck .	CR 54:1152
Unknown	D20S104	17	1	0.06	Kidnev	PNAS 92:2854
Unknown	0205104	3	0	0	Kidnev	PNAS 92:2854
Unknown	D20S117	5	0	0	Kidnev	PNAS 92:2854
Unknown	D20S117	21	0	Ö	Kidney	PNA5 92:2854
Unknown	D20S19	29	1	0.03	Kidney	CR 51:820
Unknown	D20519	39	O	0	Liver	CR 51:89
Unknown	D20S19	40	6	0.2	Lung	CR 52:2478
Unknown	D20S104	23	2	0.09	Melanoma	CR 56:589
12	D20S6	2	0	0	Neuroblastom	CR 49:1095
					a	
Unknown	Unknown	16	0	0	Ovary	CR 53:2393
Unknown	D20519	32	4	0.12	Ovary	CR 51:5118
12	D20527	.14	3	0.21	Ovary	BJC 69:429
12	D20S6	27	4	0.15	Ovary	IJC 54:546
Unknown	D20519	-5	0	C	Pancreas	CR 54:2761
12	D20S5	2	0	0	Pancreas	CR 54:2761
Unknown	D2055	6	0	-0	Prostate	G 11:530
Unknown	D20S19	8	2	0.25	Sarcoma	CR 52:2419
12	D20S5	13	4	0.31	Sarcoma	CR 52:2419
Unknown	D20519	15	3	0.2	Stomach	CR 52:3099
12	D2056	. 22	9	0.41	Testis	0 9:2245
Unknown	D20519	2	0	0	Uterus	GCC 9:119
12	D20527	26	Q	0	Uterus	CR 54:4294
12	D20S6	4	1	0.25	Uterus	CR 51:5632
NUE		684	73	0.11		
CONTRACTOR STORY	DZUSO	CONTRACTOR COMPANY NAMED IN	**************************************	THE PROPERTY OF THE PROPERTY O	Uterus	CR 51:5632

Chromosome 20 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
13.3	CSP11	20	1	0.05	Uterus	CR 54:4294
Unknown	Unknown	20	0	0	Brain	CR 50:5784
13.2	D2054 .	15	2 2	0,13	Breast	GCC 2:191
Unknown	D205119	26	3	0.12	Cervix	CR 56:197
13.2	D2094	23	7	(0,00)	Cervix	CR 54:4481 -
Unknown	D20S25	25	0	0	Endocrine	CR 56:599
Unknown	D20919-	19	-3-	0.16	Esophageal	CR 54:2996
Unknown	D20S100	18	1	0.06	Head&Neck	CR 54:4756
Unknown	D205100	× 21 ·	7	0.1	Head&Neck.	CR 54:4756
Unknown	D205110	16	1	0.06	Head&Neck	CR 54:1152
Unknown	D205119	- 11		0.09	Head&Neck	CR:54:1152
Unknown	D20S100	16	0	0	Kidnev	PNAS 92:2854
Unknown	D209100		0		Kidney	PNAS 92:2854
Unknown	Unknown	5	1	0.2	Liver	BJC 64:1083
13.2	D205€		0	0	Liver	JJCR 81:1084
13.2	D20S4	4	0	0	Liver	CCG 48:72
13.2	D2094	10	1	0.1	Lung	PN 84:9252
13.2	D2054	10	4	0.4	Lung	PN 86:5099
13.2	D2054	2	. 2	1	Lung	PN 86:5099
13.2	D20S4	6	2	0.33	Lung	PN 86:5099
Unknown	D209100	30	0	0	Melanoma	CR156:589
Unknown	D20S19	33	0	0	Ovarv	IJC 54:546
13.2	D2054	19	3 .	0.16	Ovary	CR 53:2393
Unknown	D20S46	14	3	0.21	Ovary	BJC 69:429
Unknown	D20654	14	1	0.07	Ovary	BJC 69:429
13.2	D20S4	8	0	0	Prostate	G 11:530
13.2	D2054	11.	0	0	Stomach	CR 48:2988
Unknown	D20S19	31	0	0	Testis	0 9:2245
Unknown	D20526	25	1	0.04	Testis	GCC 13:249
13.2	D20S4	36	4	0.11	Testis	0 9:2245
13.3	CSPI1	20	1	0.05	Uterus	CR 54:4294
SUM		509	38	0.07		

Chromosome 21 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Frag.	Tumor Type	Refer
11.1	D21S52	13	1	0.08	Uterns	CR 51
Unknown	Unknown	14	0	0	Brain	
22.3	D21S113	5	0.	0	Brain	CR 50
Unknown	BCEI	15	2	0.13	Breast	CR 53
Unknown	D2151	21	*1	0.05	Breast	
Unknown	D21S112	29	4	0.14	Breast	
22:3	D2US113	26	4		Breast	CR 53
22.3	D21S113	3	0	0	Cervix	CR:50
22.3	D215113	19	-	0.11	Cervix	GCC 9
Unknown	D21S212	26	2	0.08	Cervix	CR:354
Unknown	D21S265	23	0	0.08	Cervix	CR 56
Unknown	D21S267	14	1	0.07	***************************************	_CR 5
Unknown	D21S11	15	Ü	0.07	Cervix	CR 56
Unknown	D21S156	16	0	0		CEG/V
22.3	D219113	9		0.22	Endocrine	CR 56
22.3	D21S113	30	11		Esophageal	_CR(5)
22.3	D215113	20	5	0.37	Esophageal	GCC 1
Unknown	D21S262	18	0	0.25	<u> Esophageal</u>	
Unknown	DZ1S262	17.	3.	0	Head&Neck	CR 54
Unknown	D21S59			0.18	Head&Neck_	CR 54
22.3	D215113	19	5	0.26	Head&Neck	CR 54
Unknown	D21S113 D21S262	19	3	0,16	<u>Kidney:</u>	<u>.CR: 51</u>
Unknown	D215262	6	0	0	Kidney	PNAS
Unknown		16	0	0	Kidney	PNAS
Unknown	D21S267-D21S265-D21S263	19	1	0.05	Kidney	PNAS
22.3	D215267-D215265-D215263	- 6	7.	.0.33	Kidney :	PNAS
21.2-TER	D21S113	15	1	0.07	Liver	CR 51
11.1	D21519	14	0	0	Liver	CCG
22.3	D21S52	4	1	0.25	Liver	JJCR
Unknown	D215113	28	5	0.18	Lung	CR ₁ S2
22.3	D215262	23	1	0.04	Melanoma	CR 56
		6	. 0	0	Ovary	0.5:2
22.3	D21S113	12	0	0	Ovary	CR 51
22.3	D215113	25	2	0.08	Ovary	IJC 5
Unknown	D21S113-11	28	10	0.36	Ovary	CR 53
11,2	D21S120	12	4	0.33	Ovary	BUC 6
22.3	D21S167	13	7	0.54	Ovary	BJC 6
22.3-QTER	D215171	13	3	0.23	Cvary	BJC/6
22.3	D21S113	3	0	0	Pancreas	CR 54
Unknown	D2198-D21517	10	0	0	Prostate	G 11:
Unknown	Unknown	6	2	0.33	Sarcoma	CGC 5
22.3	D215113	15	1	0.07	Sarcoma	CR 52
22.3	D215113	21	3	0.14	Testis	0 9:2
22.3	D21S113	- 6	31	0.17	Dterus	GCC_9
22.3	D21S167	20	0	0	Uterus	CR 54
11.1	D21552	13		0.08	Uterus	CR251

WO 98/41648

154 / 214

PCT/US98/05419

Chromosome 21 - q Arm

SUM

692 90 0.13

Chromosome 22 - q Arm

Band	Marker	Total	Cases w/LOH	LOH Freq.	Tumor Type	Reference
11.2-13.1	TOPIP2	15	1	0.07	Uterus	CR 54:4294
Unknown	BCR	2	0	0	Brain	CGC 53:271
Unknown	CRYB	7	1	0.14	Brain	CR 50:6783
Unknown	CYP2D	6	4	0.67	Brain	CR 53:2386
Unknown	CYP2D	6	6	1	Brain	
11.2-12	D2251	4	0	0		CR 53:2386
11.2-12	D2291	7	2	0.29	Brain	CR 50:6783
11.1-11.2	D22510	5	1	0.2	Brain	CGC 53:271
Unknown	D22S156	4	2	0.5	Brain	CGC 53:271
Unknown	D22S156	4	1		Brain	CR_53:2386
13.3	D22S171	2	0	0.25	Brain	CR 53:2386
11.2	D22S20	2	0	0	Brain	CGC 66:117
Unknown	D22S23	g B	3	0	Brain	CGC 66:117
Unknown	D22S24	1		0.38	Brain	CR:50:6783
Dnknown	D22S258		0	0	Brain	CR 50:6783
Unknown		18		0.11	Brain	CR 54:1397
25.000000000000000000000000000000000000	D22S258	16	1	0.06	Brain	CR 54:1397
Unknown	D22S28	44	3	0.75	Brain	CR 50:6783
Unknown	D22S29	3	2	0.67	Brain	CR 50:6783
Unknown	D22532	2	0	0	Brain	CGC 66:117
Unknown	D22S32	14	1	.0.07	Brain	CR 49:6572
Unknown	D22S32	14	1	0.07	Brain	CR 50:5784
13.1	D22580	4	0	0	Brain	CGC 66:117
Unknown	D2299	8	2	0.25	Brain	CGC 53:271
Unknown	D2259	1	0	0	Brain	CGC 66:117
Unknown	IGLY.	2	0	0	Brain	CGC 66:117
Unknown	IGLV	1	0	0	Brain	CR 50:6783
13	IL2RB	18	4	0.22	Brain	CR'54:1397
13	IL2RB	15	0	0	Brain	CR 54:1397
11.1-11.2	LAMBDALC	4	1	0.25	Brain	CGC 53:271
12.3	MB	5	0	0	Brain	CGC 66:117
12.3	MB	1	1	1	Brain	CGC 53:271
12.3-13.1	PDGFB	1	1	1	Brain	CGC 53:271
11	Onknown	26	10	0.38	Breast	JNCI 84:506
Unknown	D22S10	16	4	0.25	Breast	GCC 2:191
Unknown	D22S113	9 "	1	0.11	Breast	CR 50:7184
Unknown	D22S9	24	4	0.17	Breast	GCC 2:191
12.3	MB	42	8	0,19	Breast	CR 53:4356
11.1-11.2	D22S10	27	2	0.07	Cervix	CR 54:4481
Unknown	D22S113	8	1	0.12	Cervix	GCC 9:119
Unknown	D22S280	20	3	0.15	Cervix	CR 56:197
Unknown	D225284	30	4	0.13	Cervix	CR 56:197
11.2-12	D22S1	11	1	0.09	Colon	N 331:273
11.2-12	D2251	12	4	0.03	Colon	IJC 53:382
11.1-11.2	D22S10	12	0	0.33	Colon	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
11.1-11.2	D22S10	13	7	0.54	Colon	S 241:961
Unknown	D22S10	29	11		***************************************	
	202010	23	11	0.38	Colon	CR 50:7166

Chromosome 22 - q Arm

Unknown	D2259	20				
Unknown	D2259	3		0.5	Colon	CR 50:7166
Unknown	D22S9	17	1	0.33	Colon	0 9:991
Unknown	IGLC	******	3	0.18	Colon	N 331:273
Unknown		30	15	0.5	Colon	CR 50:7166
Unknown	IGIC			0.18	Colon	N 331-273
SOMEONE STREET, STREET	IGLC	10	0	0	Colon	S 241:961
Unknown	IGLV	4	0	0	Colon	S 241:961
Unknown	IGLV	27	9	0.33	Colon	CR 50:7166
Unknown	IGLV ,	30	6	0.2	Colon	N 3311 274
12.3-13.1	PDGFB	10	0	0	Colon	S 241:961
Unknown	SIS	. 4	1	0.25	Colon	N: 331: 273
Unknown	D22S264	16	0	0	Endocrine	GCC 13:9
Unknown	D229351	19	1	0.05	Endocrine	
11.2-12	D22S1	21	2	0.1		CR 56:599
Unknown	D22532	13		0.08	Esophageal	CR 54:2996
Unknown	D22579	18	3	0.17	Esophageal	GCC 10:177
Unknown	D22S283	25	3	****	Esophageal	CR 51:2113
Unknown	D22S2B3	22		0:08	Read&Neck	CR 54:4756
13	IL2RB	24	2	0.09	Head&Neck	CR 54:4756
Unknown	D22S113	10	***************************************	0.29	Head&Neck	CR 54:1152
12	D225268	39	2	0.2	Kidney	CR 51:820
Unknown	D22S280-D22S282		1	0.03	Kidney	BJC 69:230
Unknown	D22S280-D22S282	22	0	0	Kidney	PNAS 92:2854
Unknown	D22S283	6	0	0	Kidney	PNAS 92:2854
Unknown	D225283	6	0	0	Kidney	PNAS 92:2854
11.2-12		16	<u> </u>	0	Kidney	PNAS 92:2854
Unknown	D22S1	10	0	0	Liver	JJCR 81:108
Unknown	D22S113	4	0	0	Liver	CR 51:89
Contraction of the contract of the	IGLC	28	9	0.32	Liver	JJCR 84:893
Unknown	IGLC	7	0	0	Liver	CCG 48:72
11.2-12	D22S1	7	2	0.29	Lung	CR 54:5643
11,2-12	D2251	22	11	0.5	Lung	CR 54:5643
11.2-12	D22S1	3	2	0.67	Lung	CR 54:5643
Unknown	D22S113	16	3	0.19	Lung	CR:52:2478
Unknown	D22S283	35	2	0.06	Melanoma	CR 56:589
11,1-11.2	D22S10	13	3	0.23	Ovarv	IJC 54:546
Unknown	D225113	10	2	0.2	Ovary	CR 51:5118
Unknown	D22S156	10	3	0.3	*****	*******************************
Unknown	D22S430-D22S282-	32	23	0.72	Ovary	BJC 69:429
······································	D22S283-D22S274			0.72	Ovary	BJC 70:905
Unknown	D2299	14	10	0.71	Ovary	CR:53;2393
Unknown	IL-2RB-CYP2D-	14	4	0.29		
	D22S156			0.29	Ovary	BJC 72:1330
12.3-13.1	PDGFB	5	1	0.2	Ovary	CR 50:2724
Unknown	SIS	6	0	C	Ovary	CR 30:2724
11.2-13.1	TOPIP2	12		0.42	Ovary	BJC 69:429
Unknown	D22S113	4	0	0.42	word the second	······································
Unknown	DZ2S156	26	20	0.77	Pancreas	CR 54:2761
			· · · · · · · · · · · · · · · · · · ·	U.//	Pediatric	GCC.15:10

Chromosome 22 - q Arm

Unknown	D22S257	20	10	0.5	Pediatric	GCC 15:10
Unknown	D22\$258	23	18	0.78	Pediatric	GCC 15:10
Unknown	D22S264	26	9	0.35	Pediatric	GCC 15:10
Unknown	D22S273	21	14	0.67	Pediatrio	GCC 15:10
Unknown	D22S273	26	16	0.62	Pediatric	GCC 15:10
Unknown	.D22S274	14	10	0.71	Pediatric :	GCC. 15710
Unknown	D225275	17	13	0.76	Pediatric	GCC 15:10
Unknown	D22S280	25	17	0.68	Pediatric	GCC 15:10
Unknown	D22S281	20	12	0.6	Pediatric	GCC 15:10
Unknown	D22S283	29	18	0.62	Pedlatric	GCC 15-10 %
Unknown	D22S301	20	14	0.7	Pediatric	GCC 15:10
Onknown	D22S303	21	12	0.57	Pediatric	GCC 15:10
Unknown	D22S315	26	18	0.69	Pediatric	GCC 15:10
Unknown	IGLV	10	0 :	0	Pediatric	CR 50:3279
12.3-13.1	PDGFB	7	1	0.14	Prostate	G 11:530
11.2-12	D2251	21	8	0.38	Sarcoma	CR 52:2419
Unknown	D22S9	6	2	0.33	Sarcoma	CGC 53:45
11.2-12	D2251	17	0	Ü	Stomach	CR 48:2988
Unknown	IGLC	7	2	0.29	Stomach	CR 52:3099
11.1-11.2	D22S10	26	6	0.23	Testis	0 9:2245
12.3-13.1	PDGFB	3	0	0	Testis	CCG 52:72
12.3-13.1	PDGFB	2	0	0	Testis	CCG 52:72
12.3-13.1	PDGFB	1	0	0	Testis	CCG 52:72
Unknown	D225113	16	3	0.19	Oterus	GCC 9:119
11.2-13.1	TOPIP2	15	1	0.07	Uterus	CR 54:4294
SUM		1594	472	0.3		

Chromosome	Arm	LOH Freq.
1	35 P * 3	0.26
1	q	0.15
2	P	0.15
2	q	0.12
3	Pi.	0.00
3	q	0.18
	P	0.15
4	ď	0.22
5	P1	0.19
3	đ	0.27
6	Р	
7	đ	0.25
7	P	0.12
8	q	0.22 (0.32
8	P P	0.14
9	Q q	0.14
9	q	0.47
10.	4	0.18
10	q	0.23
11	P	0.23
11	q	0.26
12	p	0.15
12	q	0.13
13	q	0.29
14	Р	0.08
14	я	0.22
15	p	0.11
15	q	0.17
16	P	0.17
16	g	0.36
17	p	0.44
17	q .	0.31
18	p	0.12
18	d	0:29
19 19	Р	0.13
19 20		0:3
	р	0.11
20 21	<u> </u>	0.07
21	đ	0.13
	g	V- 3

Fig. 5

1) Cyclins

Validation: Deletion of CDC23(Anaphase Promoting), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromoson	ne Genbank Sequence	
9	CDC-25A		1	3p21	U54831
10	CDC-25C		1	5g31	
524	Weel		• •	•	M34065
1043	CDC16Hs		3 .	.p15.3-p15.1	X62048
			2	13	U18291
1278	Cyclin D1		4	11q13	M73554
1280	Cyclin D3		2	6p21	M90814
1298	Cyclin H Assembly Factor		1	•	
1445	Cyclin-Dependent Protein Kinase		1	4	X87843
1450	DAN binding markets		2	12	U79269
	RAN binding protein 1		1	22	D38076
1523	14-3-3 PROTEIN TAU		1	10	X56468

1) Cyclin dependent kinases/phosphatases

Validation: Deletion of CDC28 (Cyclin Dependent Protein Kinase), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1051	CDC28 protein kinase 1		2	17	X54941
1052	CDC28 protein kinase 2		1	9	X54942
1111	Protein phosphatase 1, catalytic subunit, alpha isoform	!	4	11	M63960
1388	M-PHASE INDUCER PHOSPHATASE 2		1	20	M81934
1401	M-phase phosphoprotein, mpp6		5	7	X98263

1) Cell Division Structural Proteins

Validation: Deletion of CBF2 (Kinetochore Protein), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
20	MCM7 (Minichromosome Maintainend	:e	3 7a	21.3-q22.1	U20980
1246	Chromatin assembly factor-I p60	subunit	2	21	U20980
1273	Chromosome segregation gene homo	log CAS	1	20	U33286
1347	High-mobility group (nonhistone chromosomal) protein 1	-	5	13q12	D63874
1487	Chromatin structural protein hom (SUPT5H)	olog	3	7	Y12790
1607	Centromere protein B (80kD)		1	20p13	X05299

Validation: Deletion of SAT2(Osmotolerance), a S. cerevisiae gene in the same biochemical family, is lethal.

Name	Variances Identified	Chromoso	me Genbank Sequence	
ATPase, Ca++ transporting, plasma membrane 2	1	5	3p26-p25	X63575
ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide		4	12p13-qter	X03559
Putative Chloride Channel		1 1	3g14.3-g21.1	X83378
Copper Transport Protein HAH1		1	5	U70660
Nuclear chloride ion channel prot (NCC27)	ein	4	20	U93205
Sodium channel, voltage-gated, ty beta polypeptide	pe I,	1	19q13.1	L16242
Transient receptor potential char	nel 1	1	3	X89066
		4	j	L06328
	ATPase, Ca++ transporting, plasma membrane 2 ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide Putative Chloride Channel Copper Transport Protein HAH1 Nuclear chloride ion channel prot (NCC27) Sodium channel, voltage-gated, tybeta polypeptide Transient receptor potential char	ATPase, Ca++ transporting, plasma membrane 2 ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide Putative Chloride Channel Copper Transport Protein HAH1 Nuclear chloride ion channel protein (NCC27) Sodium channel, voltage-gated, type I, beta polypeptide Transient receptor potential channel 1	ATPase, Ca++ transporting, plasma 5 membrane 2 ATP synthase, H+ transporting, 4 mitochondrial F1 complex, beta polypeptide Putative Chloride Channel 1 1 Copper Transport Protein HAH1 1 Nuclear chloride ion channel protein 4 (NCC27) Sodium channel, voltage-gated, type I, 1 beta polypeptide Transient receptor potential channel 1	ATPase, Ca++ transporting, plasma 5 3p26-p25 membrane 2 ATP synthase, H+ transporting, 4 12p13-qter mitochondrial F1 complex, beta polypeptide Putative Chloride Channel 1 13q14.3-q21.1 Copper Transport Protein HAH1 1 5 Nuclear chloride ion channel protein 4 20 (NCC27) Sodium channel, voltage-gated, type I, 1 19q13.1 beta polypeptide Transient receptor potential channel 1 1 3

2) Antiporters

Validation: Proven essential in mammalian cells by tritium suicide selection experiments.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1471	Solute carrier family 9 (sodium/hydrogen exchanger)		1	1p36.1-p35	M81768
1250	ATPase, Na+/K+ transporting, bet polypeptide	a 1	1	1q22-q25	X03747
1251	ATPase, Na+/K+ transporting, bet polypeptide	a 2	2	17p	M81181
1605	Solute carrier family 4, anion exchanger, member 2 (erythrocyte membrane protein band 3-like 1)		2	7q35-q36	U62531

3) Acyltransferase

Validation: Essential for metabolic processes such as biosynthetic reactions and energy metabolism. The S. cerevisiae histone acetyltransferase PAT1 and the N-alpha acetyltransferase which acetylates the N-termini of proteins are essential for growth.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1227	Acetyl-Coenzyme A acyltransferase (peroxisomal 3-oxoacyl-Coenzyme i thiolase)		2	3p23-p22	X12966
1387	Lysophosphatidic acid acyltransferase-alpha		7	6	U56417

3) Amino Acid Biogenesis

Validation: Deletion of PRO1(Glutamate 5-Kinase), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1330	Glutamic-oxaloacetic transaminas soluble (aspartate aminotransfer	ase 1)	1 10q2	24.1-q25.1	M37400
1331	Glutamic-oxaloacetic transaminas mitochondrial (aspartate aminotransferase 2)	e 2,	2	16q21	M22632
1447	Pyrroline-5-carboxylate syntheta (glutamate gamma-semialdehyde synthetase)	se	1	10q24.3	X94453

3) Amino Acid Transport

Validation: There are ten essential amino acids in man, which must be transported across the plasma membrane for use in protein synthesis.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1581	Solute carrier family 3 (cystine dibasic and neutral amino acid transporters, activator of cysti dibasic and neutral amino acid transport), member 1		2	2p16.3	L11696
	dibasic and neutral amino acid	ne,			

3) Addition, removal, or modification of phosphate groups

Validation: Deletion of CMD1(Calmodulin), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1269	Calcineurin A catalytic subunit		2	8	S46622
1270			1	10q21-q22	M30773
1351	TRECORDOR		1	10q21-q22	M84739
1432	SERINE/THREONINE PROTEIN PHOSPHI 2B CATALYTIC SUBUNIT, BETA ISOF		2	10	M29551
1476			1		U83236

3) GDP Dissociation Inhibitors

Validation: Deletion of GDI1(GDP dissociation Factor), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified		Sequence	
			2	14023-024	D13988

3) Lactate Transport

Validation: Genes required to maintain organic compounds at levels required for cell growth or survival.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1583	Solute carrier family 16 (monocarboxylic acid transporter member 1	rs),	2	1p13.2-p12	L31801
	• • • • • • • • • • • • • • • • • • • •				

3) Polyamine Biosynthesis

Validation: Inhibition of polyamine biosynthesis has antiproliferative effects as demonstrated by inhibitors of polyamine metabolism.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1587	Ornithine decarboxylase 1		2	2p25	M16650

3) Protein Glycosylation

Validation: Deletion of DPM1(Dolichol-phosphate mannosyltransferase), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1328	Glutamine-fructose-6-phosphate transaminase		1	2p13	M90516
1339	Heparan Heparan Heparan Heparan N-deacetylase/N-sulfotransferase	<u>-2</u>	2	10	U36601
1434	UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferas		3	18	U41514

3) Protein Kinase C

Validation: Deletion of PKC1(Protein Kinase C), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1440	Terretain the state of beca i		4	16p11.2	X06318
1443	The state of the s		1	10p15	L01087
1444	Protein kinase C substrate 80K-H		1	7	J03075
		• • • • • • • • • • • • • • • • • • • •			

3) Protein Post-modification

Validation: Deletion of BET2(Geranylgeranyltransferase), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name		Variances Identified	Chromosome	Genbank Sequence	
1081	geranylgeranyl transfe beta-subunit	erase type	II	2	1	X98001

3) Sugar Biosynthesis and Processing

Validation: Deletion of PGI1(Glucose-6-phosphate Isomerase), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances	Chron	osome	Genbank	
		Identified			Sequence	
	DID 5 Winner 1 .					
1220	PIP 5 Kinase beta		2		9q13	X92493
1229	Aconitase 2, mitochondrial		1	22q11	.21-q13.3	U80040
1249	ATP SYNTHASE ALPHA CHAIN,		2		18	D14710
1252	MITOCHONDRIAL PRECURSOR					
1257	, Cransporting,		3		18	X60221
	mitochondrial F0 complex, subuni isoform 1	tb,				
1258	January III, Cransporting,		5	2102	2.1-q22.2	X83218
	mitochondrial F1 complex, O subu	nit	-	4-	2.1.q22.2	X0321B
	(oligomycin sensitivity conferri protein)	ng				
1302		rase	5		11	AF001437
	(E2 component of pyruvate		_		**	AFOUL437
	dehydrogenase complex)					
1303	Dihydrolipoamide dehydrogenase (E3	5		7g31-g32	J03490
	component of pyruvate dehydrogen	ase	•		7431-432	003490
	complex, 2-oxo-glutarate complex					
	branched chain keto acid dehydro	, Genage				
	complex)	50				
1346	Hexokinase 1		3		10-22	W75.56
1366	Isocitrate dehydrogenase 2 (NADP	٨١	2		10q22	M75126
	mitochondrial	*//	2		15q26.1	X69433
1395	NADH dehydrogenase		1			
1421		uhuni +	4	10-11	2p16	X81900
1422	B13		*	rabii	.31-p11.2	U53468
1422		-S	1	18p11	.31-p11.2	U65579
	protein 8, 23 kDa subunit precur (NDUFS8)					
1424	NADH-UBIQUINONE OXIDOREDUCTASE 7 SUBUNIT PRECURSOR	5 KD	3		2	X61100
1427		al bara	9			
1430	Phosphofructokinase	e) Deta			3p13-q23	M34479
1451			1		21q22.3	M10036
	COMPLEX 11 KD PROTEIN PRECURSOR		3		1,3	M36647
1464	(Ip) subunit	lphur	3	lpi	22.1-qter	D10245
1465	flavoprotein (Fp) subunit		10		5p15	D30648
1576	Pyruvate kinase, liver		2		1g21	D10326
1577	Oxoglutarate dehydrogenase (lipo	amide)	6		7p14-p13	D10523
1579	Acyl-Coenzyme A dehydrogenase, v	erv	3	17011	.2-p11.13	D43682
		•	-	- / 1/11	- P	243002

	long chain			
1584	Dihydrolipoamide S-succinyltransferase	5	14g24.3	L37418
1588	Acyl-Coenzyme A dehydrogenase, C-4 to	1	1p31	M16827
	C-12 straight chain		-2	
1590	Pyruvate kinase, muscle	4	15g22	M23725
1596	Phosphoglucomutase 1	5	1031	M83088
1603	Phosphofructokinase, muscle	4	12a13.3	U24183
1611	Enolase 3, (beta, muscle)	1	17pter-p12	X16504

3) Sugar Transport

Validation: Genes required to maintain organic compounds at levels required for cell growth or survival.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1594	Solute carrier family 2 (facility glucose transporter), member 5	ated	3	1p31	M55531
1598	Solute carrier family 5 (sodium/glucose cotransporter),	member 2	ı	16	M95549
		•••••••			

4) Protein Degradation

Validation: Deletion of CDC48(Ubiquitin proteolysis), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1027	26S PROTEASE REGULATORY SUBUNIT	4	3	14	L02426
1037		•	1	11	
1098		rtial	6	9,19	X04366 D50913
1114	Proteasome (prosome, macropain) subunit, beta type, 6		7	9,19	D29012
1115		tz,	4	9	D38048
1116	PROTEASOME COMPONENT C13 PRECURS	OR	2	9	U17496
1117			6	1	D26599
1118	Human mRNA for proteasome subuni pll2, complete cds	t	2	2	D44466
1119		t p27,	1	2	AB003177
1289	ATP-DEPENDENT CLP PROTEASE PROTE SUBUNIT	OLYTIC	2	19	Z 50853

4) Protein Folding

Validation: Deletion of HSP10(Chaperonin), a S. cerevisiae gene in the same biochemical family, is lethal.

WO 98/41648 PCT/US98/05419

1287	DEDMINIC DAGGE			
1287	PEPTIDYL-PROLYL CIS-TRANS ISOMERASE, MITOCHONDRIAL PRECURSOR	1	10	M80254
	DNAJ PROTEIN HOMOLOG 2 DNAJ PROTEIN HOMOLOG HSJ1	1 2	9,2 9,2	D13388 X63368

4) Ribosomal Subunit

Validation: Deletion of GRC5(Ribosome), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Ide	riances Chromosom	s Genbank Sequence	
1127	H. sapiens mRNA for ribosomal protein	T11 2		
1128	Ribosomal protein L17	L11 3	9,2	X79234
1130	60S RIBOSOMAL PROTEIN L18A	5	17,4	X52839
1131	Ribosomal protein L19		3	X80822
1133	60S RIBOSOMAL PROTEIN L23A	1	17q11	X63527
1135	Human ribosomal protein L27a mRNA,	2	17,18	U43701
	complete cds	3	6,11	U14968
1136	TIDOSOMAI DIOCEIN LZB MRNA	11		
	complete cds	11	19	U14969
1137	mended process 132	4		
1138	Human ribosomal protein L35 mRNA,	3	20	X03342
	complete cds	3	20	U12465
1139	Process Land	1	3-22	
1140	Human mRNA for ribosomal protein Lag	, 2	3q29-qter	X52966
	complete cds	2	3q29-qter	U57846
1141	process L4	4		
1142	Ribosomal protein L6	1	3,6	L20868
1143	Ribosomal protein L7		12	X69391
5	Ribosomal protein L7A	1	12	L16558
1144	Ribosomal protein L8	5	19q33-q34	M36072
1145	Ribosomal protein L9	2	12	Z28407
1146	Ribosomal protein, large pi	2 5	12	U09953
1147	Human ribosomal protein S10 mRNA,	1	15,22	M17886
	complete cds	1	20	U14972
1148		2		
1149	40S RIBOSOMAL PROTEIN S15	1	19q	X06617
1150	40S RIBOSOMAL PROTEIN S15A	. 2	19q	J02984
1151	Ribosomal protein S16		19q	X84407
1152	Ribosomal protein S17	5	19	M60854
1154	40S RIBOSOMAL PROTEIN S23		11pter-p13	M13932
1155	Ribosomal protein S25	2	5	D14530
1157	Ribosomal protein S28	2	11q23.3	M64716
1158	40S RIBOSOMAL PROTEIN S29	2	19	U58682
1159	Ribosomal protein S5	1	19	L31610
1160	40S RIBOSOMAL PROTEIN S7	2	19	U14970
1161	Ribosomal protein S9	3	19	M77233
1223	Ribosomal protein L7a	3	19	U14971
	> Process Big	6	9q34	X52136

4) T-Complex

Validation: Deletion of CCT2(T-Complex), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name			Variances Identified		Semience	
1489	T-COMPLEX	PROTEIN 1,	ALPHA	SUBUNIT	1	6	S70154

T-COMPLEX PROTEIN 1	3 2	5 1	D43950 X74801
 	 		

4) Translation Elongation

Validation: Deletion of CDC33(eIF4e), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1063	Eukaryotic translation elongation factor 1 delta	n	3	7	Z21507
1073	Eukaryotic translation initiation factor 4A (eIF-4A) isoform 2	on	1	18p11.2	D30655
1095	Human mRNA for KIAA0031 gene, co	omplete	3	17,2	D21163
1099	Human mRNA for KIAA0219 gene, pa cds	artial	3	12	D86973

4) Translation Factor

Validation: Deletion of CDC33(eIF4e), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1049			2	12	X81625

4) Translation Initiation Factors

Validation: Deletion of CDC33(eIF4e), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1068	Human translation initiation factories plid subunit gene	tor	1	16	U46025
1069	_	LIKE	1	17	D21853
1070	Eukaryotic translation initiation factor 4C (eIF-4C)	n	3	1,X	L18960
1072	Eukaryotic translation initiation factor 2A	on	2	14	J02645
1074	Eukaryotic translation initiation factor 4E	n	3	14	M15353
1312	Translation initiation factor 3 (eIF-3) p36 subunit		1	12	U39067

4) tRNA Synthetases

WO 98/41648 PCT/US98/05419

Validation: Deletion of ALA1(Alanyl-tRNA synthetase), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1031	Alanyl-tRNA synthetase		2		
1040	Cysteinyl-tRNA synthetase		2	16q22	D32050
1079	Glycyl-tRNA synthetase		1	11p15.5	L06845
1090	Toolousis the		2	7p15	U09510
1102	Isoleucine-tRNA synthetase		2	9921	D28473
	ASPARAGINE SYNTHETASE		3	- 4	M27396
1121	Arginyl-tRNA synthetase		3	Ennau -11	
1198	Threonyl-tRNA synthetase		•	5pter-q11	S80343
1218	VALYL-TRNA SYNTHETASE		1	5p13-cen	M63180
1221			4	9	X59303
	TRYPTOPHANYL-TRNA SYNTHETASE		1	14	M61715

4) Ubiquitin and Ubiquitin Associated

Validation: Deletion of UFD1(Ubiquitin Fusion), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1309	Ubiquitin carrier protein (E2-EP)	·			
1315	Cyclin-selective ubiquitin carrie	.)	2	17	M91670
	protein	er	2	17	U73379
1362	UBIQUITIN CARBOXYL-TERMINAL HYDRO	T.ASE 3	2		
1363	UBIQUITIN CARBOXYL-TERMINAL HYDRO	TACE M	-	14	D80012
1420	UBIQUITIN CARBOXYL-TERMINAL HYDRO	MASE I	1	12	X91349
1431	IBIOUTIN CARRONIC TERMINAL HYDRO	LASE 14	4	13	M68864
	UBIQUITIN CARBOXYL-TERMINAL HYDRO	LASE	2	4	X04741
1511	Ubiquitin A-52 residue ribosomal protein fusion product 1		1 19	9p13.1-p12	S79522
1514	Ubiquitin-conjugating enzyme E2I		б		
1515	Ubiquitin fusion-degradation prot	- #	-	16p13.3	U45328
	(UFD1L)	ein	4	18	U64444

5) DNA Helicases

Validation: Deletion of DNA2(DNA Helicase), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1050	Human CHL1 potential helicase complete cds	(CHLR1),	3	18	U33833
1057	ATP-DEPENDENT DNA HELICASE II, SUBUNIT	86 KD	ı	2	M30938
1123 1397	RecQ protein-like (DNA helicas 218kD Mi-2 protein	e Q1-like)	2 1	12p12-p11	L36140 X86691
			_		

Validation: Deletion of POL2(DNA pol epsilon), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence		
1059	subunit mRNA, complete cds		3	12	U21090	
1105	DNA polymerase alpha subunit		1	X,11	L24559	

5) DNA Replication

Validation: Deletion of CDC45(Chromosomal DNA Replication), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosom	e Genbank Sequence	
1048	DNA REPLICATION LICENSING FACTOR HOMOLOG	CDC47	1	4	D55716
1094	Human mRNA for KIAA0030 gene, parcds	rtial	2	3	X67334
1124	Replication factor C (activator : (145kD)	1) 1	2	4p14-p13	L14922
1208 22	DNA topoisomerase I Topoisomerase II			20q12-q13.1	J03250
1222	Minichromosome maintenance defici		2	17q21-q22	J04088
	(S. cerevisiae) 3	lent	1	17q21-q22	D38073
1461	Replication protein A2 (32kD)		2	1p35	J05249

5) Histone

Validation: Deletion of CSE4(Similar Histone H3), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1335			3	22	X03473
1336	······································		3	22	D64142
1341 1342	HISTONE H1D HISTONE H2A.1		5	6	X57129
1343			4	6	U90551
1344			1	6	L19779
1345			1	1	M60756
			1	1	X60486

5) Polyadenylation and 3' Cleavage

Validation: Deletion of FIP1(Polyadenylation Factor), a S. cerevisiae gene in the same biochemical family, is lethal.

1053	Human cleavage and polyadenylation specificity factor mRNA, complete cds	1	11	U37012
1349	HNRNP METHYLTRANSFERASE	4	14	D66904
1426	Poly(A)-binding protein-like 1	2	14	Y00345

5) Purine/Pyrimidine Biosynthesis

Validation: Deletion of CDC8(Thymidylate Kinase), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
					_
1235	ADENYLOSUCCINATE LYASE		1	1	X65867
1268	CAD PROTEIN			•	
1293	CTP synthetase		÷	4	D78586
1326			2	lp34.1	X52142
	formyltransferase, phosphoribosylglycinamide synthe phosphoribosylaminoimidazole syn	etase,	4	21q22.1	X54199
1437	Phosphoribosyl pyrophosphate amidotransferase		2	4q12	U00238
1510	Thymidylate synthase		2	18p11.32	X02308
1517		rase	2	3q13	J03626
1518			1	7	X90858

5) Ribonucleotide Reductase

Validation: Deletion of RNR1(Ribonucleotide Reductase), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1452	RIBONUCLEOSIDE-DIPHOSPHATE M1 CHAIN	REDUCTASE	4	11	X59543

5) RNA Helicase

Validation: Deletion of BRR2(RNA Helicase), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1100	Human mRNA for KIAA0224 gene, co	omplete	4	16	D86977
1163	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 9 (RNA helicase A)	;	1	1	L13848
1484	PUTATIVE ATP-DEPENDENT RNA HELIC STE13	ASE	3	19	U90426

WO 98/41648 PCT/US98/05419

5) RNA Polymerase II Components

Validation: Deletion of RPA135(RNA pol Subunit), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1026	"" Dupicus (Clone mr. 18) bys		 3		
	polymerase II mRNA, complete cde		3	19	L37127
1088	Human RNA polymerase II subunit (hsRPB10) mRNA, complete cds		7	19	U37690
1109	RNA polymerase II, polypeptide C	(23kp)			
1110	Polymerase (RNA) II (DNA directed	(33KD)	3	16q13-qq21	J05448
	polypeptide A (220kD)	1)	1	17p13.1	X63564
1165	DNA-DIRECTED RNA POLYMERASE II 23 POLYPEPTIDE	KD KD	9	17p13.1	J04965
1360	RNA polymerase II subunit hsRPB7		1	11	U20659
			••••		

5) RNA Polymerase III

Validation: Deletion of RPA135(RNA pol Subunit), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1170	Human RNA polymerase III subunit (RPC62) mRNA, complete cds		1	11	U93867

5) RNA Splicing/Processing

Validation: Deletion of CUS1(U2 snRNP protein), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromoso	ome Genbank Sequence	
1171	The state of the s	ein /	1	2	U41371
1172	(SAP 145) mRNA, complete cds Human splicesomal protein (SAP 61 mRNA, complete cds)	3	2	U08815
1176		r	1	22	X85237
1177	Splicing factor, arginine/serine-	rich 2	2	4,17	W00104
1181	Human splicing factor SRp30c mRNA complete cds	,	1	4,17	M90104 U30825
1183	PRE-MRNA SPLICING FACTOR SRP75		2		
1216	SPLICING FACTOR U2AF 65 KD SUBUNI	-	2	1	L14076
1224	Human (clone Es 1) Pro Sci SUBUNI	I .	1	1	X64044
	Human (clone E5.1) RNA-binding pr mRNA, complete cds	otein	4	1	L37368
1322	Fibrillarin				
1354	Heterogeneous nuclear		1	1	X56597
	ribonucleoprotein K		1 9q	21.32-q21.33	S74678

1455	U1 SMALL NUCLEAR RIBONUCLEOPROTEIN A	3	9q21.32-q21.33	X06347
1460	U1 small nuclear RNP-specific C	2	15	X12517
1473	SnRNP core protein Sm D3	2	22	U15009
1474	SnRNP core protein Sm D2	5	22	U15008
	Ul snRNP 70K protein	3	19913.3	M22636
1478	Small nuclear ribonucleoprotein polypeptides B and Bl	3	20	J04564
1480	Small nuclear ribonucleoprotein polypeptide N	5	15q12	U41303

5) TATA-Binding Proteins

Validation: Deletion of TAF145(TAFII Complex), a S. cerevisiae gene in the same biochemical family, is lethal.

Name	Variances Identified	Chromosome	Genbank Sequence	
H.sapiens mRNA for transcription factor TFIID subunit TAFII28	1	1	6	X83928
Human TFIID subunit TAFII55 (TAF mRNA, complete cds	TIISS)	1	5	U18062
TATA box binding protein		2	6a27	M55654
TBP-associated factor (hTAFII130))	1	20	U75308
-	H.sapiens mRNA for transcription factor TFIID subunit TAFII28 Human TFIID subunit TAFII55 (TAF mRNA, complete cds TATA box binding protein	H.sapiens mRNA for transcription factor TFIID subunit TAFII28 Human TFIID subunit TAFII55 (TAFII55) mRNA, complete cds	H.sapiens mRNA for transcription 1 factor TFIID subunit TAFII28 Human TFIID subunit TAFII55 (TAFII55) 1 mRNA, complete cds TATA box binding protein 2	H.sapiens mRNA for transcription 1 6 factor TFIID subunit TAFII28 Human TFIID subunit TAFII55 (TAFII55) 1 5 mRNA, complete cds TATA box binding protein 2 6927

5) Transcription Elongation Factors

Validation: Deletion of RPO21(RNA pol Subunit), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name		• • • • • • • • • • • • • • • • • • • •	Variances Identified	Chromosome	Genbank Sequence	
1077	TRANSCRIPTION	ELONGATION	FACTOR	S-II	4	В	M81601
4	TRANSCRIPTION	ELONGATION	FACTOR	B3	5	5q31	L34587
32	Elongin TCEB1				3	1p36.1	L47345

5) Transcription Factors

Validation: Deletion of BBP1(BFR1p binding), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
33	SUPT6H		3	17q11.2	U46691
1202	Human TFIIA gamma subunit mRNA, complete cds		1	15	U14193
1205	General transcription factor TFI beta subunit, 34 kD	IE.	1	8p21-p12	X63469
1206	TRANSCRIPTION INITIATION FACTOR BETA SUBUNIT	IIF,	1	8p21-p12	X16901
1247	CYCLIC-AMP-DEPENDENT TRANSCRIPTI FACTOR ATF-1	ON	1	19p13.3	X55544
1248	CAMP-dependent transcription fac	tor	3	2	M86842

	ATF-4 (CREB2)			
1274	Transcription Factor (CBFB)	1	2	1 20200
1292	CRM1 protein	3	-	L20298
1368	Transcription Factor IL-4 Stat	_	2	Y08614
1373	CICNAL MANAGEMENT THE STATE	1	21q21-q22.1	U16031
13/3	SIGNAL TRANSDUCER AND ACTIVATOR OF	1	21q21-q22.1	M97935
	TRANSCRIPTION 1-ALPHA/BETA			
1411	THE THE THE THE THE THE THE THE THE THE	1	19	U85193
1483		1	17	U48730
1496	Transcription factor 12 (HTF4,	2	= :	
	helix-loop-helix transcription factors 4)	-	15q21	M83233
1497	Transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47)	8	19p13.3	M31523
1498	Transcription factor 6-like 1 (mitochondrial transcription factor	1	7p	M62810
	1-like)			
1500	TRANSCRIPTION FACTOR P65	3	11	710057
1501	Transcription factor COUP 2 (a.k.a.	2		L19067
	ARP1)	2	15q26.1-q26.2	X91504

6) Clathrin

Validation: Deletion of RET1(Alpha-Cop), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1242	CLATHRIN COAT ASSEMBLY PROTEIN	AD47			
1243			2	8	D38293
	CLATHRIN COAT ASSEMBLY PROTEIN	AP50	6	3	U36188
1282	procetti		5	22	X83545
1290		.L.\			
	Clarker, trans botybeboude (FG	:D)	1	4q2-q3	M20470
1291	Clathrin heavy chain		4	17q11-qter	U41763
-					

6) Cytoskeleton

Validation: Deletion of MHP1(Microtubule Interacting), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name .	Variances Identified	Chromosome	Genbank Sequence		
1	Actin, gamma Subunit					
			8	17p11-qter		X04098
	Sh3p17(Myosin IC Heavy Chain)		1		21	U61166
1032	fetal brain, mRNA, 1452 nt]		4	20		S65738
1038	Capping protein (actin filament) gelsolin-like	•	3	2cen-q24		M94345
1039	Human capping protein alpha mRNA partial cds	.,	2	7		U03851
1056	Desmin		1	2q35		J03191
1080	Gelsolin (amyloidosis, Finnish t	vne)	1	-		X04412
1092	Keratin 19	1PC)	5	9q34		
1093	KERATIN, TYPE II CYTOSKELETAL 6D		-			Y00503
1267			13	5,12		J00269
			1	2		X82207
1284	- the master		5	11q13		X95404
1383			1	20		M13451
1385	Lamin B receptor		1	1q42.1		L25931

1386	MYOSIN LIGHT CHAIN ALKALI, NON-MUSCLE ISOFORM	1	12,17	M22920
1404	MYOSIN HEAVY CHAIN 95F	1	4-16 5	
1405	MYOSIN HEAVY CHAIN IB	•	4p16.3	U90236
1406	Myosin-IC	1	13	D63476
1486	SUPPRESSOR OF TUBULIN STU2	1	13	U14391
1495	MICROTUBULE-ASSOCIATED PROTEIN TAU	1	11	X92474
1507	Tubulin, gamma polypeptide	1	17	J03778
1508	TUBULIN ALPHA-4 CHAIN	1	17	M61764
1520		1	17	X06956
1320	Myosin VIIA (USH1B)	2	17	U39226

6) ER Protein

Validation: Deletion of BET1(v-SNARE), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1272 1317 1614 1615	Calnexin ER LUMEN PROTEIN RETAINING RECEIRIBOPHORIN I Ribophorin II	PTOR 2	1 1 4 1 2	5q35 19 3q 0q12-q13.1	M94859 M88458 Y00281 Y00282

6) Integrin

Validation: Deletion of MYO2(Myosin Heavy Chain), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1378	Integrin alpha-3 subunit		1	5q23-q31	M59911

6) Karyopherin

Validation: Deletion of KAP121(Karyopherin), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1091 1214	karyopherin alpha 3 transportin (TRN)		3	13 13	D89618 U70322

6) Lysosomal Proteins

Validation: Essential for sequestering and degrading aged or defective organelles and polymers that can interfere with cell survival, proliferation as seen by human diseases such as Tay-Sachs disease.

ID	Name	Variances Identified	Chrom		Genbank Sequence	
1265	ATPase, H+ transporting, lysosom (vacuolar proton pump) 31kD	al	2	22pt	er-q11.2	X76228
		•				

6) MITOCHONDRIAL IMPORT

Validation: Genes required to maintain inorganic ions at levels compatible with cell growth or survival.

ID	Name			Variances Identified	Chromosome	Genbank Sequence	
1578	MITOCHONDRIAL TOM20	IMPORT	RECEPTOR	SUBUNIT	8	1	D13641

6) Nuclear Pore Complex

Validation: Deletion of GSP1(Nuclear Pore Trafficking), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
28	Nuclear Pore Complex NUP214				
29	Nucleoporin 98		3	9	D14689
1266	HETEROGENEOUS NUCLEAR		3	11p15	U41815
	RIBONUCLEOPROTEIN C		4	20	L38696
1350	Heterogeneous nuclear ribonucleoprotein A1		4	12q13.1	X79536
1355	Nuclear pore complex protein hou	p153	3	6	Z25535
1425	NUCLEAR PORE GLYCOPROTEIN P62	-	1	-	
1449	Export protein Rael		-	11	X58521
1454	HETEROGENEOUS NUCLEAR		5	20	U84720
	RIBONUCLEOPROTEINS C1/C2		3	12	M29063
1524	140 KD NUCLEOLAR PHOSPHOPROTEIN		5	10	D21262

6) Protein Transport

Validation: Deletion of BET3(v-SNARE associated), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
8	Integral Transmembrane Protein				
1467	Sec23A isoform		3	11q23-24	L38961
1608			2	14	X97064
1000	Signal recognition particle rece ('docking protein')	ptor	8	11q23-q24	X06272
1613	TIM17 preprotein translocase		2	1	X97544

Validation: Deletion of SED5(Syntaxin), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name		Variances Identified	Chromosome	Genbank Sequence	
1186	syntaxin	1A				
1188	syntaxin	3		1	21q22.1	L37792
1189	-			1	11	U32315
1190	,			2	11	U26648
	Syncaxin	,		1	6	U77942
			•			

6) Vacuolar Protein

Validation: Deletion of PPA1(Vacuolar H-ATPase), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1261	Vacuolar H+ ATPase proton channel subunit	1	2	6	M62762

6) Vesicle Proteins

Validation: Deletion of SAR1(COP II), a S. cerevisiae gene in the same biochemical family, is lethal.

ID	Name	Variances Identified	Chromoso	me Genbank Sequence	
1025	Human (chromosome 3p25) membrane protein mRNA		3	3,18	L09260
24	COATOMER BETA SUBUNIT		•	_	
1055	COATOMER DELTA SUBUNIT		•	3	X70476
1082	Human GP36b glycoprotein mRNA,		8	11	XB1198
	complete cds		3	5	U10362
1173	SEC14 (S. cerevisiae)-like		~ .		
1174	Human homologue of yeast sec7 mRN	· •		7q25.1-q25.2	D67029
	complete cds	А,	2 1	7q25.1-q25.2	M85169
1184	Human chromosome 17q21 mRNA clone	T 20112	_		
1217	H. sapiens mRNA for vacuolar-type	PLITZ	1	17	U18009
	H(+)-ATPase 115 kDa subunit		2	17	Z71460

99) Direct Essential Yeast Homolog

Validation: Deletion of the S. cerevisiae homologue of this gene is lethal.

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1238	Aldolase A		2		
1239	Aldolase B, fructose-bisphosphate		_	16q22-q24	M11560
1241	C. adams 2, liuctose-Disphosphate	!	2	9q22	X02747
	S-adenosylmethionine decarboxylas	e 1	1	6q21-q22	M21154
1271	Calmodulin 1 (phosphorylase kinas delta)	e,	1	14q24-q31	D45887
1300	DED81		1	18	U79254

1301	Deoxyhypusine synthase	3	19p13.11-p13.12	L39068
1306	Dolichol monophosphate mannose	2		
	synthase (DPM1)	•	20	AF007875
1318	ESS1 PROTEIN	7	19	******
1332	Glucose phosphate isomerase	•		U49070
1333		1	19q13.1	K03515
	Guanylate kinase (GUK1)	3	19913.1	L76200
1359	Heat shock 60 kD protein 1 (chaperonin)	1	- 9	M34664
1367	PERIODIC TRYPTOPHAN PROTEIN 1	1	-	
1372	IPP isomerase	-	12	L07758
		1	10	X17025
1396	N-acetylglucosaminyltransferase I	4	5q31.2-q31.3	M55621
1399	Mannose phosphate isomerase	3		
1414	Nipl	-	15q22-qter	X76057
	• -	1	5	U15172
1415	GLYCYLPEPTIDE N-TETRADECANOYLTRANSFERASE	2	17	M86707
1433	PHOSPHATIDYLINOSITOL 4-KINASE ALPHA	10	17	
1446	PERIODIC TRYPTOPHAN PROTEIN 2		= :	L36151
1519	_	2	8	U53346
1313	Uridine diphosphoglucose	1	2	U27460
	pyrophosphorylase		-	

F18,6

Target Variances by Field Table for Conditionally Essential Genes

Conditionally Essential Biosynthetic Enzymes

Validation: Conditionally Essential

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1536	5-methyltetrahydrofolate-homocys methyltransferase	teine	3		U75743
1539	Glutamate-ammonia ligase (glutam synthase)	ine	5	1q31	X59834

Proteins that Repair Radiation Induced DNA Damage

Validation: Conditionally Essential

ID 	Name	Variances Identified	Chromosome	Genbank Sequence	
1541	Fanconi anemia complementa	tion group C	1	9q22.3	X66894

Proteins of DNA Repair

Validation: Conditionally Essential

ID	Name	Variances Identified	Chromosome	Genbank Sequence	
1528 1530 1532 1533 1537 1526	DNA excision repair protein ERCC HHR23A protein DNA EXCISION REPAIR PROTEIN ERCC DNA repair helicase ERCC3 URACIL-DNA GLYCOSYLASE 1 PRECURS Damage-specific DNA binding prot (127 kD)	-1 OP	4 3 2 19q1 1 2 2	13q33 9 3.2-q13.3 2q21 8 11, 15	D16305 D21235 M13194 M31899 X15653 AJ002955

Proteins that repair chemically induced DNA damage

Validation: Conditionally Essential

ID	Name				
	- · — · · •	Variances	Chromosome	Genbank	
1534	0-6-methylquanine_nwa	methyltransferase	OHI OHO SOME	Gemank	
	1-3-2-11C-DUV	metnyitransierase	4	10-26	1450050

Fig. 7

		F 19.	I		
Target	Loc'n	Sequence around	# Varia 1	# Varia 2	Protein
ID		[polymorphism]	(Lib)	(Lib)	Change
1.01 .02	472 250	CGGCCATGTA (C/T) GTGGCCATCC	71 (36)	1 (1)	Silent
.02	1003	ACGAGGCCCA [G/A] AGCAAGCGTG	71 (36)	1 (1)	Silent
.04	801	CGGGCATTGC [C/T] GACAGGATGC ACGAGCTGCC [C/T] GATGGCCAGG	66 (35)	6 (5)	Silent
.05	1201	AATGCTTCTA [A/G] ACGGACTCAG	71 (36) 71 (36)	1 (1)	Silent
.06	991	CCACCATGTA [C/T] CCGGGCATTG	71 (36) 17 (17)	1 (1)	Silent
.07	1099	TGTGGATCGG [T/C] GGCTCCATCC	71 (36)	56 (35) 1 (1)	Silent Silent
.08	499	GTGCTGTCCCT [C/G] TACGCCTCT	65 (65)	7 (7)	Silent
	·				
4.01	2168	CCGCCAGTAG[C/T]ATCAGCTTTA	61 (34)	11(9)	3'UT
.02	388	TGGAAAGCCA (C/T) GGGGAGCCGA	62 (29)	10(7)	Thr->Met
.03	491	agagagaga (t/c) gagagaaaga	68 (36)	4(4)	Silent
.04	1171	AAAACTAATT [T/C] GGATAGAAAG	68 (36)	4(4)	Leu->Ala
.05	336	TCGGGATGCC[C/T]TGCAGAAGGA	71 (36)	1(1)	Silent
5.01	421	ACGTCCCAAC[G/A]AAGAGACCAC	66 (36)	6 (6)	Silent
		*			Silent
8.01	1570	CTCCGTCCA [T/C] TGTACTATCTG	70 (36)	2(2)	Silent
.02	778	TCCACGTCCT (C/G) GTGCTGATGC	71 (36)	1(1)	Silent
.03	158	GGACACACTT [T/C] TGAAGCTTCT	71 (36)	1(1)	Silent
0.01					
9.01	1929	CCATGCACCA (C/A) GAGGACTTTA	71 (36)	1(1)	His->Gln
10.01	1099	AACCGTGTCAGGGAAACACCA	69 (36)	3 (3)	Gly->Arq
	• • • • • • •	••••••			GIY-MIG
14.01	911	CAATTCAATC [G/A] CCGCCCTAAA	69 (36)	3 (3)	Arg->His
.02	1174	CAAACAGTAA [G/A] TGAAAATGGT	71 (36)	1(1)	3
					• • • • • • • • • • • • • • • • • • • •
20.01	1627	CCCAGCACAT [C/T] ACCTATGTGC	44 (30)	28(21)	Silent
.02	2041	GCCGAAGTGT[C/G]CGGTTCTCTG	71 (36)	1(1)	Asp->Glu
. 03	1393	cagccatcca(c/t)gaggtcatgg	71 (36)	1(1)	Silent
22.01	4008	CAACAAAAAC [A/C] AAATTCACAA	71 (26)		0:3
.02	4446	AGCCATCCAC [T/G] TCTGATGATT	71 (36) 71 (36)	1(1) 1(1)	Silent Silent
				* \ * / *	3116110
24.01	1101	GCCACTGGCA [G/A] TAAAGGATAT	71 (36)	1(1)	Val->Ile
28.01	5009	TGCCACGCCC [G/C] TGTTTGGGCA	70 (36)	2(2)	Val->Leu
.02	2023	AGAAATCACC [C/T] AGGATAACCC	71 (36)	1(1)	Silent
. 03	2041	CCCCTCCAGC [G/A] GCAAAGCCAG	71 (36)	1(1)	Silent
29.01	1768	CCCTGCCACT (A/C) GAGTCCGGCC	67 (36)		6/1
.02	2781	AGGAGCATCC [G/A] TCTAAAACTA	70 (36)	5 (5) 2 (2)	Silent Silent
.03		2 bp deletion	70 (307	2(2)	3'UT
32.01	1171	AAAACTAATT[T/C]GGATAGAAAG	70 (36)	2(2)	Leu->Ala
.02	388	TGGAAAGCCA [C/T] GGGGAGCCGA	59(33)		Pro->Met
.03	2168		60 (34)	12(10)	
33.01	2397	CCCTACATCC [T (a) creaces >>>	47/22)		
.02	3708	GGCTAGATGG [T/C] CTGGCCAAAA AGGTCGGGGT [C/T] GATGTCAACC	47(33)		Silent
.03	3795	GGACCCACCT [C/A] CTGAAGATCC	63 (35) 62 (35)	10/0) Silent
	1598	CACAAGTTGA (G/A) GAGGGCGATA	68 (36)	4 (4	4) Silent
.02	2548	CACAAGTTGA (G/A) GAGGGCGATA CTTATATTTC [T] ¹⁰ GATGTCAACC	71 (36)	1(1) 3'UT
.03	3158	AAAATTGTCT (GTTT) GTTTTCTCAT	50 (34)	22 (2)	דטינ (ס
525.01			54 (34)		6) Silent
.02	346 523				Leu->Phe
		······································		9 (9	
1025.01				48 (44)	
			•	,,	

.11	418	GCCCCTTTTG [C/T] AGCCCACGGC	6 (5)	5 (3)	N/D
.12	640	CAACTAACCA [G/A] ACAACTGGGA	15 (7)	7 (6)	N/D
1026.2					
.9	47	GTCTGGACGC [G/A] ACGGCGGCGG	2 (2)	3 (2)	5' UT
.19	262 602	CCCACCCCTT [G/A] GAGCACAAGA	28 (13)	4 (1)	Silent
.19	602	ATAAAGTATAGCGG (a/g) agagan	S (5)	11 (8)	3' UT
1027.2	405	TCCAACAGE (# /e) amount of			
.6	405 942	TGGAAGAGAT [T/C] ATTGATGACA	2 (2)	2 (2)	Silent
.16	1361	GGACAAAAAG [A/G] TATGACTCCA	8 (8)	4 (4)	Silent
.16	1361	CAGGAAGGCA [C/A] CCCTGAGGGG	13 (11)	3 (3)	Thr -> Asn
1031.31	2990	CCTTCCCCCA (a /) amagagaman			
.32	2991	CCTTCGCCCA [G/A] CTGCGCCTCG CTTCGCCCAG [C/G] TGCGCCTCGG	9 (7)	2 (2)	Silent
		TITEGECEAG (C/G) IGCGCCICGG	4 (4)	4 (4)	Leu -> Val
1032.1	3	AGTCGCCG [G/A] GGAGGACGGTCT	F / 4\		
.2	4	GTCGCCG [G/A] GAGGACGGTCTGC	5 (4) 5 (5)	3 (3)	5' UT
.3	69	CCGCCGCGC [G/A] AAGATGGCCT		3 (2)	5' UT
.10	312	AAAAAGATTG [T/C] CGCTATGCTT	5 (5)	2 (2)	5 UT
			8 (8)	3 (3)	Silent
1037.20	2919	TGGTTATGGG [G/C] GTGCCAGAGG	15 (13)	2 / 2\	
			13 (13)	2 (2)	3' UT
1038.5	723	CAGGTCCTGG [G/C] CCCCAAGCCT	7 (7)	3 (3)	Silent
.10	862	ACTCCAGCCC [C/A] TTTGCCCTTG	5 (5)	13 (10)	Silent
.13	1053	CCTCAGGGCC [G/A] TGAGAGTCCC	13 (10)	8 (7)	
					Arg -> His
1039.19	1665	ACCATGTCTC [A/G] GTTTATTTTT	2 (2)	6 (5)	יט יצ
.23	1748	TATTTGAGTA [G/A] AAAATCACTT	3 (3)	2 (2)	3' UT
				- (-,	
1040.7	2056	GCTGAAGAAG [T/C] CTTCGAGGCT	20 (16)	2 (2)	3' עד
1043.1	351	ACTTGAAGGA (T/C) GAAAGTGGCT	2 (2)	3 (3)	Silent
. 2	372	TCAAAGATCC [C/T] TCCAGCGACT	2 (2)	3 (3)	Silent
1048.3	341	GCTACGCGAA [G/A] CTCTTTGCTG	2 (2)	2 (2)	Silent
1049.10	2648	CCTGAAACCC [T/A] GAAGCTGATG	5 (4)	3 (1)	מי עד
.12	2768	Cagtggtagc [g/a] atggaaaaa	8 (6)	2 (1)	3' UT
1050 11					
1050.11	2381	CAGGAAGAAG [A/G] TATTCCAGGA	4 (2)	2 (2)	Ile -> Val
.13	2750 3034	TTTTGCCAGC [G/A] TAGTGCTCCT	2 (2)	2 (1)	Val -> Ile
.14	3034	GAGTCCAGAG [T/C] GCTGCCAGGA	2 (2)	2 (1)	3' UT
1051.10	260	AGCTGGCAAG [C/T] TACTTTTCAG	15 (10)		
.18	409	TTTGCTTCTT [G/A] AGTAGAGCCA	15 (10)	3 (1)	3' UT
			17 (12)	3 (1)	3' UT
1052.7	428	TGTACAAATC [T/C] TTCATCCATA	7 (6)	2 (2)	3 1777
			, (0 /	2 (2)	3' UT
1053.24	4113	AGGAGAAGAC [C/T] TACCGGCGGC	8 (7)	8 (8)	Silent
			,		
1055.17	3122	CAGCGTCAGC [C/A] AGCTCAGCCT	4 (4)	4 (4)	3' UT
.23	3450	TGAGAAGGC [T/C] TGGGACAAGA	26 (12)	3 (3)	3' UT
.25	3568	TCAAAAAACC[T/C]TTTTTTCTG	26 (12)	2 (2)	3' UT
.01	2061	AGGCTGGTCG [C/T] GAACTCCTGA	61 (34)	11(9)	זטי נ
.02	2419	TTAAAAGATA [C/A] GCATGTCTTC	59 (33)	13(10)	3'UT
.03	3047	TAAGTCTTTT [G/T] AGTGTCATCA	71 (36)	1(1)	3'UT
.04	2960	TATTACTCAC [G/A] TATACCCCAT	71 (36)	1(1)	3 י ט י
.05	3450	TGAGAAGGGC [T/C] TGGGACAAGA	60(33)	12(9)	דטי נ
.06	3296	CTGCAAAGAG [T/C] GTACTGTGCT	60 (33)	12(9)	3'UT
1056.12	407	CAAGAGCACC [G/C] GTGGGGCCCC	13 (9)	2 (2)	Val -> Arg
1057.20	3067	TAACTTTTCG [G/A] TCTTTCCCAT	7 (5)	3 (3)	3טינ
1059.11	1130	AACGTGAGTG [A/G] CATTTTCCGA	5 (5)	2 (2)	Asp -> Ala

Target	Loc'n	Sequence around	# Varia	1 :	# Varia 2	Protein	
ID		[polymorphism]	(Lib)		(Lib)	Change	
.1	9 1327	AATCATCCGA [G/A] GTCC	TGAGGA	19	(14)	3 (3)	Val -> Ser
. 2	7 1474	GGGAGGCCTG [G/A] GGCT	GGCCC	15	(11)	2 (2)	Gly -> Arg
1063.2	1 705	CGGACATGGC [C/T] CAGC	TGGAGG	8	(7)	8 (7)	Silent
. 2	2 721	GGAGGCCTGT [G/T] TGCG	CTCTAT	16	(14)	2 (2)	Val -> Leu
. 3	8 949			2		2 (2)	3' UT
1068.3	0 2756				(15)	2 (2)	Ala -> Arg
1069.1	0 1199	• • • • • • • • • • • • • • • • • • • •			(13)	2 (2)	Arg -> Glu
1070 3							
1070.3					(2)	6 (6)	Gly -> Val
.7					(6)	2 (1)	Silent
.1	2 1092	2 GAAGTCTGCA [G/T] TTGA		5		3 (3)	3' UT
1072.2	0 1309						
.2				15		2 (2)	3' UT
						5 (5)	3' UT
1073.2						2 (2)	Silent
					(1)	2 (2)	SITERC
1074.1				5	(4)	2 (2)	3' UT
.2				_	(6)	3 (3)	3' UT
. 2					(5)	3 (3)	3' UT
						J (J/	
1077.1	9 127	5 TATAATAATT [G/T] TATG	GTACCT	3	(2)	3 (3)	3' UT
. 2	2 158				(5)	3 (1)	3' UT
. 3	0 233				(3)	10 (9)	3' UT
. 3	4 246				(4)	16 (14)	3' UT
1079.1	1 203	5 CTGCTGTAGT [T/C]GCTC	CATTCA	19	(14)	2 (1)	Silent
. 1	.8 234	7 GCAACATCAC (A/G) TGGG	CTGATG	25	(17)	2 (2)	Silent
1080.2	4 236	7 TGCCTGAGGA [A/C] GGGC	AGGCC	1	(1)	5 (4)	3' UT
1081.1					(8)	2 (1)	Ser -> Lys
.3	6 117	8 ATGCATATTGTAAAATAAA	(A/G)A	2	(2)	10 (9)	3' UT
1082.1					(5)	2 (2)	Ser -> Phe
. 4					(3)	3 (3)	Asp -> Glu
.,		3 GTCTACAGAT [G/T] GGCT	GIGGCC	4	(4)	5 (5)	3' UT
1088.3	1 11	2 CCGAGGGGGA [C/T] GCG	TCCATC	22	(16)	7 (5)	Silent
.1					(18)	/ (5) 5 (4)	Cys -> Ser
.1					(16)	5 (4)	Cys -> Trp
.2					(16)	18 (11)	3' UT
. 2					(19)	3 (3)	3' UT
	24 27				(18)	9 (6)	3' UT
	27 33				(15)	2 (2)	3' UT
1090.1	18 415				(12)	2 (2)	3' UT
.:	21 421				(16)	2 (1)	3' UT
1091.3	3 79	3 AGGATCCCCC (A/G) CCG	CCTATGG	2	(1)	5 (2)	Silent
. 9	9 96	2 CTTTCTTGTG [C/T] CCC	TCTGAG	4	(3)	5 (2)	Pro -> Ser
.:	14 207	8 AAGAGGTGCA (A/G) TGTC	GATCTGA	6	(5)	11 (8)	3' UT
1092.5		• • •			(8)	4 (1)	Ala -> Pro
	10 40	* * * *				11 (5)	Silent
	11 50	*			(6)	6 (5)	Silent
.:	22 103	4 TTGGAGCCCA [G/C] CTG	GCGCATA	4	(4)	3 (2)	Gln -> His

Target ID	Loc'n	Sequence around [polymorphism]	# Varia :	1 #	Varia	2 Protein	
							• • • • • • • • • • • • • • • • • • • •
	3 103		CGCATAT	3 (3)	3 (2)	Leu -> Val
1093.2		CTCTCACAGA [C/T] GAG					
.3					2) 2)	2 (1) 3 (2)	Silent
. 4	33:				2)	3 (2)	Silent Silent
.6	420		CGGGCTG	3 (3 (2)	Silent
. 2:	2 954			7 (-	3 (1)	Val -> Ala
.2			TCCAGCA	7 (2)	3 (1)	Silent
.24				7 (2)	3 (1)	Silent
. 2				7 (3 (1)	Ile -> Thr
.2				9 (3 (1)	Silent
. 4				13 (3 (1)	3' UT
. 4:				13 (14 (4 (1) 5 (2)	3' UT
. 5	158			13 (6 (3)	3' UT 3' UT
1094.2				15 (9)	4 (2)	מי טיד
	5 3104		TGGCCAG	2 (2)	4 (2)	3' UT
1005 1							
1095.1				18 (11)	2 (2)	Silent
	1 324				10)	3 (3)	3' UT
			AAGGGGC	10 (12 (11)	3י דט
1098.1					7)	3 (3)	Ala -> Pro
.13	3 152				1)	12 (10)	Asp -> His
. 2			ACTCAAT :		6)	2 (2)	3' UT
. 2				21 (13)	2 (2)	3' UT
. 2		, . , . , . , , ,		16 (6 (,5)	זט ינ
. 3		CCAAGGAGCG [C/A]GCT		13 (10)	2 (2)	3' UT
1099.3							
.3	-				11) 8)	6 (4) 6 (4)	3' UT
. 4					12)	9 (8)	3' UT 3' UT
.0:	1 21			53 (3		9(9)	
.0:	2	Nucleotide rep	eat	66 (35)	6 (5)	3 'UT
1100.1					3)	4 (3)	3' UT
.1		, . , . ,			2)	4 (3)	3' עד
	2 4040				6)	6 (5)	3' UT
				, ,		5 (5)	3 ' UT
1102.2	9 196	TAACTTGGGT [T/G] TGA	AAAAAAT	2 (1)	25 (20)	3' UT
. 3		AAAAATAAAA [T/G] TCC	TAAATTT	2 (1)	24 (20)	3' UT
.3	1 199:	AAAAATAAAATTCCTAAA	T [T/C] T	2 (1)	21 (17)	3' UT
			•				
1105.1	5 2031	GGGCCTGCCT [G/C] TGA	GTGGTGC	3 (3)	6 (6)	מט יצ
1109 4	00	AGCTTGCCTG[C/T]TTC					
		AGCTTGCCTG[C/T]TTC	AGCAAAA	4 (4) 	2 (1)	3' UT
1110.1	1 646	CTGATGCAGA [T/C] TCT		5 (5 (5)	3' UT
						J (J)	3. 01
1111.8				2 (7 (6)	Silent
. 1	5 108			8 (4 (4)	3' UT
.1		CCCGACCCCT [A/C] AGG	CCCACCT	3 (1)	18 (17)	3' UT
.1				22 (4 (4)	3' UT
		ATCOMN COMN (C./m) CCC					
1114.1	-				16) 15)	2 (2)	
.2					15)		Asn -> Lys
. 2					12) 14)		Ala -> Ser Ala -> Val
.0:				70 (3		2(2)	Silent
.0:				71 (3		1(1)	Pro->Ala

.03		GGCCGGAGGC [A/G] TTCACTCCAG	30(20)	42 (32)	Silent
1115.2	77	ACTGCCGCAG [G/A] AATGCCGTCT	13 (9)	4 (1)	Silent

Target	Loc'n	Sequence around	# Varia	1	# Varia	2 Protein	
ID		[polymorphism]	(Lib)		(Lib)		
.5	130		AAAACT	8	(7)	14 (4)	Val -> Ala
.1			TCCGGA		(8)	2 (1)	Leu -> Pro
.10	5 732	CAAGAAGGGG [A/C] CCAG	GCTTGG	12	(7)	4 (2)	Thr -> Pro
1116.2	12:	CCC3.CCCMCC.(= / 1) c =					
.3	173		ACAGTT		(1)	4 (4)	Silent
		CCGGGGAATG [A/C] AGCC	CACAGA	2	(1)	5 (5)	Lys -> Gln
1117.1	19	CCTGCAGCCC [T/C] GGCC	TTCCCC		·		
.2	16				(7)	4 (3)	5' UT
.5	19				(7) (7)	4 (3)	5' UT
.1					(7)	2 (2) 8 (4)	5' UT
.0:	1 128				36)	7(7)	Leu -> Phe
.0:	2 3389				36)	2(2)	Ser->Val 3'UT
							3 01
1118.5	1683	GACATGGTTG [G/A] TTAT	GCACAA	6	(5)	2 (1)	Val -> Asp
.2	8 2945				(6)	7 (5)	3' עד
1119.1	1 1075	TCACAAATTA [G/A] GCCA	CGGCCC	3	(3)	3 (3)	3' UT
1121.1					(3)	2 (2)	Silent
.2:				6	(6)	3 (3)	Ala -> Pro
.2	7 1902	GACAGACTGG [G/A] AAAA	TATTGA	2	(2)	20 (17)	Gly -> Glu
1123.9	2489						
.1					(5)	4 (4)	Asn -> Thr
		TTGACATAAC [T/C] ATCT	TITTGA	4	(3)	3 (3)	3' טד
1124.2	119	TCTTATCGGA [G/A] CTTG	ሚስ ውርጥር		())		
.7	3616				(1)	3 (3) 5 (3)	5' UT
					(1/	5 (3)	Ala -> Ser
1127.2	4	TGCAAAA [G/A] CGCAGGA	TCAAGG	13	(8)	2 (1)	Ala -> Thr
.1	5 79				(14)	2 (1)	Silent
.3	4 339		TGGGTA		(2)	31 (16)	Silent
1128.9	483			4	(3)	4 (3)	3' UT
.10	0 484	AAATAAAAAAAAA (A/T)	AAACCC	4	(3)	4 (3)	3' UT
1130.7	248			25	(12)	9 (4)	Val -> Leu
.1:				26	(12)	2 (1)	Asp -> Tyr
.13					(10)	3 (2)	Met -> Ile
.10					(B)	4 (3)	Arg -> Ala
	7 42,	TGGAGGAGAT [C/T] GCGG	TCAGCA	12	(7)	2 (1)	Silent
1131.1	2 502	TGGCTGACCA[G/A]GCTG	ACCCCC	10	(13)		043
		· · · · · · · · · · · · · · · · · · ·		19	(13)	2 (2)	Silent
1133.20	279	CTGAGTCTGC [C/T] ATGA	AGAAGA	41	(18)	2 (1)	Silent
.3					(12)	4 (2)	3' UT
						- \ - /	
1135.2					(20)	B (4)	Silent
. 2	3 343		TTCTGG		(18)	4 (2)	Silent
.3:		AAGAGTGTTG [G/A] GGGG	GCCTGT	32	(18)	2 (2)	Gly -> Ser
1136.1				9	(9)	10 (6)	יפ יד
.10				31	(21)	5 (4)	Ala -> Thr
.11					(23)	5 (5)	Silent
.1:					(16)	8 (5)	Ala -> Glu
.2:					(20)	5 (5)	Lys -> Asn
. 24					(20)	5 (5)	Pro -> Ala
.29					(22)	6 (3)	Pro -> Leu
.2:					(18)	5 (5)	Ala -> Pro
.3:					(18)	5 (5)	Ala -> Val
.4:					(22)	2 (2)	Arg -> Cys
. 4.		TCCTGCGCAC [G/C] CAGA	MUCCIG	2	(2)	19 (14)	Silent

			 -						
Target ID	Loc'n	Sequence around [polymorphism]		aria : Lib)	1	# Varia (Lib)		Protein Change	
1137.1		CTTCCTTC [G/T] AGGA							
.1!			-			(2)		3 (2)	5' UT
. 2:						(12) (9)		4 (2)	Silent
. 29						(8)		3 (2)	Leu -> Val
		· · · · · · · · · · · · · · · · · · ·	CIGGENIC			(0)		4 (4)	3' UT
1138.8	78	AGGAGGAGCT [G/T] CTO	GAAACAGC		30	(17)		2 (2)	Silent
. 14				_		(15)		2 (2)	Ala -> Thr
. 24						(16)		2 (2)	Silent
						(10)		2 (2)	Silent
1139.2	1 334	TTCCGAAGCA[A/G]TC	TCCTGCT		33	(20)		3 (1)	Asn -> Ser
1140.3	17	CCGCTGCTCG[C/A]CA	ייייייייייייייייייייייייייייייייייייייי		22	(15)		3 (2)	5' UT
. 20						(16)		2 (2)	
					. . .			2 (2)	3' UT
1141.5	201	ATCAGACTAG [A/T] GC	TGAGTCTT		2	(1)	7	1 (5)	Arg -> Ser
.7	346					(3)		3 (2)	His -> Asn
.18	1073	GGATAAGGCA [G/A] CTO	GCTGCAGC			(4)		6 (3)	Silent
. 2	1 1376	TGTTATACAGGCAGTGA	[G/A] AAA	. 1		(10)		5 (4)	3' UT
					-				
1142.13	556	CTTGTGACTG [A/G] CC	rctggtcc		8	(7)		3 (3)	Asp -> Ala
1143.1	7 470	ATCTACAAGC[G/T]TG	STTATGGC	3	32	(20)		2 (2)	Arg -> Leu
1144.1	211	GCCGCGGCGC (G/C) CCC	CCTCGCCA		7	(5)		4 (4)	Silent
. 5	286					(9)		5 (4)	Ala -> Glu
. 6	287					(13)		4 (3)	Ile -> Phe
.1	7 494					(8)		2 (2)	Pro -> Ser
. 26						(18)		2 (2)	Silent
								- (~,	
1145.18	3 395	GTGAAAAATA [C/T] ATG	CCGCAGGG	2	21	(14)		7 (7)	Silent
. 20	405	CATCCGCAGG[G/T]TTC	CGGATGAG	2	27	(20)		2 (2)	Val -> Phe
1146.16	276	TGTTTGCAAA [G/T] GC	CCTGGCCA	1	16	(12)		3 (3)	Lys -> Asn
.18					13	(10)		5 (5)	Silent
. 23	340	ACCTGCTCCA [G/C] CAC	SCTGGTGC	1	16	(12)		3 (3)	Ala -> Pro
. 23		CCTGCTCCAG [C/G] AGG	CTGGTGCT	1	5	(12)		3 (3)	Ala -> Glu
.29	343	TGCTCCAGCA [G/A] CTC	GTGCTGC	1	7	(12)		2 (2)	Ala -> Thr
1147.22	2 324	GAGACTGGCA [G/A] GC	CTCGGCCT		7	(5)		3 (3)	Arg -> Lys
1148.29	390	TCGGTGACAT[C/T]GT	CACAGTGG	3	3	(17)		3 (2)	Silent
1149.14	174	CANCECCCC (a /a) mc/	20000022						
				-		(12)		3 (2)	Leu -> Val
. 22	2 414					(20)		4 (3)	Ala -> Cys
1150.20	257	CTCAAAGACC[T/C]GG/							
.34		CCTCATGGAC [T/A] AAJ				(6)		2 (1)	Leu -> Pro 3' UT
								4 (3)	
1151.13									
. 14						(16)		6 (1)	Leu -> Pro Silent
.16						(16)		2 (1)	
. 22						(14)		6 (4)	Ala -> Val
. 25				_		(15)		3 (1)	
1152.19						(18)			Ser -> Lys
. 19		• • • • • • • • • • • • • • • • • • • •		_		(18)			
.20						(16)		5 (3)	Lys -> Asn Leu -> Val
. 24						(9)	2	2 (15)	Silent
. 31						(23)		2 (2)	Silent
	. 							- , -,	
1154.8	119	GGGCACAGCC [C/T] TAX						3 (2)	Silent

Target ID	Loc'n	Sequence around [polymorphism]	# Varia (Lib)	1	# Varia (Lib)	2 Protein Change	
. 3	9 477	TAGTAATAAA [T/C] TTT	CATATGC	21	(15)	2 (2)	3' UT
1155.6	64	TATTCTCCGA [G/C] CTT					
.7	65				(19)	3 (3)	5' UT
			JCAAIGC	25 	(17)	3 (3)	5' UI
1157.3	75	TGGGCAGGAC [C/G] GGT	TCTCAGG	18	(11)	3 (3)	Silent
.13	2 290				(12)	11 (7)	3' UT
				 -	- 		
1158.4	55	CGAAAATTCG [G/A] CCA	GGGTTCT	36	(20)	2 (1)	Ala -> Asp
1159.2	68	ACCA CCA CCA (a /m) mag					
.7					(14) (10)	2 (1) 5 (3)	Val -> Leu
	• • • • • • • •					5 (3/	Gly -> Glu
1160.1	0 124	TCAGGGAGCT [G/A] AAT	ATTACGG	28	(18)	2 (1)	Glu -> Lys
.1			GCTATCA	28	(17)	2 (2)	Glu -> Lys
.1	7 229	TCCAAGTCCG[C/G]CTA	STACGCG	2	(2)	29 (19)	Pro -> Ala
1161.8	263	NACCON 2000 (5 /m) cma					
.9					(16)	2 (2)	Silent
.1:					(14) (9)	9 (9) 4 (4)	Silent Arg -> Pro
						* (*/ 	A19 -> F10
1163.8	1522	GTACTTCCTC [G/T] TCC	ICATGCC	2	(2)	5 (1)	Arg -> Leu
1165.1		222222222222222222222222222222222222222		- -			
.4	97 180				(3)	2 (2)	Ala -> Arg
.7	273				(3)	4 (2)	Silent Ala -> Glu
. 8	274				(12)	3 (2)	Ile -> Phe
.13	3 429				(7)	5 (4)	Silent
. 1				5	(5)	8 (5)	Leu -> Phe
. 2					(10)	4 (3)	3' UT
.3:					(5)	4 (4)	3' UT
		GATGTTTTGA [C/G] GAA	ATAAATT	2	(2)	7 (6)	3' UT
1170.2	410	ATTGCGAATC [G/C] TTA	GATATCC	2	(2)	2 (2)	Val -> Leu
1171.2	7 2823	AAGAGATGAA [A/T] AAAA			(6)		
				. .	(6)	4 (4)	3' UT
1172.1				7	(7)	2 (1)	3' UT
.1:				3	(3)	2 (2)	3' UT
. 2	5 2423	GAGAGACTGG [T/A] GGG	ICTGTCT	7	(6)	5 (4)	3' UI
1173.1	2 4730	AGTAGGTAGG [G/T] CTA			(6)		3 ' UT
. 0:					(18)	2 (1) 48(30)	Silent
. 0:					(36)	1(1)	
. 0	3 2400				(36)	1(1)	Silent
. 0		4 bp deletic					
. 0:		CTAGATAGCA [A/G] ATAG			(36)	1(1)	זטי 3
. 0		CCCAAGCTGC [C/T] TCA			(36)	9 (9)	דטי 3
1174.2		TGTTGACAGG [G/C] TTT				2 (2)	3' UT
. 2	7 3302	TCTGCCCAAGC (A/C) AA	AAAAAA	5	(3)		
1176.1	3 2571	GAGGCTTTGC [C/T] TTG	CCTGCAT	6	(4)	3 (3)	3' UT
		CTCTTCCCCC [T/C] AAA				3 (3)	3' UT
. 2	1 1864	GTTAGCTTTA [A/G] AAA	AAAAAA	5	(5)		
1181.8	678	TACCAAAGCA [G/A] GGG	TCCCCA	10	(7)	2 (2)	Arg -> Lys
		CTTCCTGCTC (G/A) ACTO					3' UT
	1 1799	TGGCTTTCAG [G/C] CCT	GCCTTT	15	(10)	5 (4)	

186 / 214

		GCCTAAATGT [G/T] TGAAGTGCGA	30 (18)	_		3' UT
1186.7	1337	GGGAGAGGTG [A/G] CCCTGAGGGA	2 (1)	4	(3)	3' UT
1188.7		AGTCATCTGA (G/A) GTTATGCTTT				

	- 		·			·				
Target ID	Loc'n	Sequence around [polymorphism]	# Varia (Lib)	1		Varia 2 (Lib)		tein nge		
1189.1	3 1270	CGGAAAGGAA [G/A] CGTTGG	CAGC		, ,	·		2 2 1		
.10					(1:			2)	3' UT	
						• <i> </i>	2 (1)	3' UT	
1190.5	1010	GGGGTTGGGC[G/T]GGTTC	TTTG	2	{ :	2)	3 (3)	3' UT	
1193.1	79	CTCTCCCCTC [C/G] AATCCT	TATCC	5	{ !	5)	2 (2)	5' טד	
1196.2	3 2123	TATGTTTTCC [T/C] ATGCAN	TAGT	19	(14	1)	2 (2)	3' UT	
1198.2	9 2399	TGGCAAAGTC[T/C]GAAATA	AGGTC	20	(15	5) 	4 (2)	זט ינ	
1199.3 .1:	1012 3 1460				(:		2 (2) 2)	Silent 3' UT	
					- - -					
1202.7	671 	L ACCATAACTT (T/C) TTTTTA	VAGGA	13	(;	7) 1	.1 (6)	זט ינ	
1205.1	942	GGAGAAAATT [G/A] AAGAAT	TATCT	13	(6	5)	2 (1)	Glu ->	Lys
1206.3	740	ACATCACAAA [A/G] CAACCT	GTGG	3	(3	3)	2 (1)	Silent	
1208.3	1984	TATTCCGTAC [G/A] TACAAT	acer		,					
. 1					(]		2 (Silent	
						., .	.5 (0)	דטינ	
1214.9	1566	GCATCCTGGA[C/T]AGCAAC	LAAGA	5	(3	3)	2 (2)	Silent	
1216.8	202	AGCGGAGCGC[C/G]TCCCGG	GACA	5	(4	1)	3 (2)	Silent	
1217.3	2545	GCCTCTCGGC [C/T]TTTCTC	CACG		(3		2 /	7\	Cilant	
. 5	2688				(6		2 (Silent 3' UT	
						, , . 				
1218.10	2757	GCAGGCTGCC [C/T] TTTAGA	GAGG	4	(2	2)	2 (1)	Silent	
. 0 :	1100				(36)			1(1)	Gly->Se	r
. 02	2 1287				(36)			1(1)	Silent	
. 03	3 3385	TTGCCTGGAC [G/A] TTGGCC	TGCG	71 ((36)			1(1)	Silent	
1221.20	1893	TGGAGCCTTC[G/T]GCTGGA	AGTC	9	(7	7)	3 (2)	3' UT	
1222.30	2797	CACAAACCCA [A/G] TTGTAA	ATAA	14	(11	L)	2 (1)	3' UT	
1223.3	2813	AAGCAGGAGG [C/T] TAAGAA	BCTC		(10	·				
.9	3662				(2	•	2 (N/D	
.10		• • • • • • • • • • • • • • • • • • • •			(4	-	3 (N/D N/D	
.15					(15		2 (=	N/D	
.16	5 4110					7)			N/D	
	4155	CGACGTGGAT [C/T] CCATCG		21		_		2)	N/D	
1224.13	3 1739	GCAGAGCCAC [C/A] AGGGAA	AAGT	2	(2	2)	2 (2)	3' UT	
.17	7 1936	CCTCTTCTAA [T/C] CTCAAG	GGTC	3			В (7)	זט יצ	
	2061	GCGAGTGAGT [G/T] GAGAGC AGCTCTGCGG [A/G] GTCATC	CAGC	15				13)	3' UT	
	2079	AGCICIGCGG [A/G]GICATC	ACGC	15	(11			13)	3' UT	
		AGAAGGTGAA [C/A] CCCCTG			,			2)		Tue
. 16	1207	TGGGAAGAGG [G/C] CATACG	CACT	9	(1)				Asn ->	-
								2)	Ala ->	PLO
1229.18	3 1919	ACTCCGTGCG[C/T]AATGCC	GTCA	4	(3	1)			Silent	
1235.11	1194	TAGCCGCCAG [G/A] ATTGCC	ATGA	18	(12	2)	2 (2)	Asp ->	Asn
1238 14	1122	AGAACCTGAA [G/A] GCTGCG	CACC		,	`				
.17	7 1298	AACAACTCCA [G/A] GCCCTG	cccc	8	(6	;)		2) 1)	Silent 3' UT	
1239.13	1289	ACTITICCTC [T/C] AATCCT	GGAA	11	(5	5)	7 (4)	3' UT	

.14 1292 TTTCCTCTAA (T/C) CCTGGAAATT 16 (7) 2 (~2) 3 -UT

Target ID	Loc'n	Sequence around [polymorphism]	# Varia (Lib)		#	Varia 2 (Lib)		otein inge		
1241.1	3 1802	AATTAAAGTTTTTCTTC[C/1] ATG	10	(7)	2	(2)	3' UT	
1242.1	8 3296	TCCTGTCACA[T/C]GTGCAG	CAGG	13	/1	11)		(2)	זטינ	
.2						7)		(3)	זטי 3	
					·	''	. 			
1243.5	134	GAACGCAGTG [G/A] ATGCCT	TTCG	4	1	4)	3	(3)	Asp ->	Agn
. 6	184				-	7)		(2)	Silent	
.7	189					7)		(2)	Val ->	Phe
. 2	4 152	CGGTGGAGCA [G/A] CCCCTG	GGCT .	10	-	-		(2)	מטיב	
.3	1 1789			14	-			(2)	3' UT	
.3	2 179	ACACGTGTTG [C/A] TTCGTC	CAGT	16				(7)	3' UT	
		• • • • • • • • • • • • • • • • • • • •								
1246.6	151	ATCCCGGAGG [G/T] TCACTC	TGAA	2	(2)	2	(1)	Val ->	Phe
. 9	195	ACGTTTTAAC [A/G] TAGTAA	ATCC	3	(3)	6	(6)	זטינ	
		• • • • • • • • • • • • • • • • • • • •	· 			·				
1247.6	51	GCGGACAGTA [C/T] ATTGCC	CATTG	2	(2)	2	(2)	Silent	
						•				
1248.4	16			4	(3)	2	(2)	Silent	
. 5				2	(1)	3	(3)	Pro ->	Gln
.1	1 81	AGCACAGCCC [C/T] TCTACC	CAGGG	13	(7)	2	(2)	Silent	
1249.1		• • • • • • • • • • • • • • • • • • • •				3)		(2)	5' UT	
	6 180	TTGTAAAAGG [G/T] TTACTO	CTCAT	26	()	L6)	2	(1)	3' UT	
1250 1	35:	GCCCGCCAG[G/A]ATTAAC				·				
1250.1		GCCCCGCCAG (G/A) ATTAAC	ALAG	3	(2)	2	(2)	Silent	
1251.1	1 107	CCGCCAACGG[C/A]AACATO	CACC			1)	4	(2)	Ala ->	C1
.1						1)		(2)	3' UT	Giu
					· .	_, 			3 01	
1253.7	67:	GCCAGGTGGT [G/C] CAGATO	CCTG	2	ı	2)	2	(1)	Silent	
.1						2)		(1)	Ala ->	Asp
.1						2)		(1)	Silent	· F
.1	6 342					2)		(1)	Silent	
. 2	1 384	GACCCCGCTG [C/T] CACCCC	GCTTT	2	(2)	2	(1)	3' UT	
1255.1	1 89	TCAAATGAAT (C/G) AACCA	CCTGG	2	(2)	2	(1)	Gln ->	Glu
. 2			GCTGC	2	(2)	17	(8)	3' UT	
.2		• • • • • • • • • • • • • • • • • • • •		2	(2)	17	(8)	3' UT	
. 2	7 180	TTTCCAATAAAATC [G/A] G	AATTC	3	(2)	3	(3)	3' UT	
1257.1						6)		(1)	Silent	
.1						14)		(2)	3' UT	
. 2		5 TGAGAGAACG [A/C] AATCTC	TATC	19	(.	14)	3	(2)	3' UT	
1258.1	1 32	9 ATCACAGCAA (A/G) AGAGAG	במידיר	22		9)	4	(1)	Lys ->	Ara
.1						10)		(3)	Silent	A LY
.1		7				11)		(1)		Phe
.2						13)		(1)		
.3						10)		(1)	3' UT	
			• • • • • • • • •			<i>-</i>		·		
1261.6	42	5 CTGGCATCAT[C/T]GCCATC	CTACG	9	(3)	2	(1)	Silent	
	0 90	* * *				3)		(3)	3' UT	
1265.1	4	ACTCGAGCCT [G/A] CTGTTC	CACCG	3	(2)	2	(1)	5' UT	
.1	9 102	GGAGGGGGCA [A/G] ATGGT	GTTG	2	(1)		(7)	3' עד	
1266.1				2	(2)	3	(2)	Glu ->	Lys
.7		-				6)		(3)	3' UT	
. 9						9)		(3)	זט יצ	
.1	6 86	5 GTAGAGCACA (G/A) GGGTT	rcccc	25	(12)	2	(2)	3' UT	

										_
Target ID	Loc'n	Sequence around [polymorphism]	# Varia (Lib)	1	#	Varia 2 (Lib)		otein ange		-
1267.11	1776	GGCTAGAGGA [T/C] GCAC	GTGGC	2		-		(5)	3' UT	-
1268.10	6529			10		6)		(2)	Thr -	- > Ile
1269.19 .20			GTGCA	12			3	(3)	3' UT	-
				12	(- - -	4) 	4	(4)	3' UT	_
1270.11	331	TTGTCCTCAG [T/C] ACCTC	TCCGT	11	(9) 	2	(2)	5י עד	
1271.14	949	GGGTGTATTA [T/C] CCAGC	STACTC	18	(1	1) 	5	(1)	3' UT	-
1272.10	2678	TGTTAAGGAA [C/T] GCTAG	CAGGG	3	(1)	3	(1)	זטינ	•
1273.13	3127	AAAGGAAGTT[T/C]TCCTT	TTGAA	7	(2)	10	(3)	3 ' UT	-
1274.16	2696 	ATATTTTTTC [A/G] TAATC	ТАТАТ	7	(6)	3	(2)	3' UT	-
1278.7	864	to to to to to tal overto	CCTCC	3	(1)	2 ((2)	Silen	- -
.32			GCTTA	5	(3)		3)	3' UT	-
.33			CTTAC		(4 (4)	3' UT	
		TGTTGTGTGT (A/G) TCGAG		10 		7) 	3 (2)	3' UT	
1280.5 .15	1648 1957	TTAAGAGGAC [G/A] TAATG TAAAGATGATTGTGG [G/A]		14		•		3)	3' UT	
		TAMONIGHTIGIGG (G/A)	AATTC	2 	(:	2) 	9 (8)	3' UT	_
1282.1	2155	TTTGGTGGGC [C/T] TACTT		7	(:	3)	6 (1)	3' UT	-
.2	2283	GTGTGGCGTA [G/C]GCAGT	GGGTC	13	(:	1)	2 (3' UT	
.9 .10	2799	TTACATCACC [G/A] CCACT	ACTGC	6	(:	3)	2 (2)	3' UT	
.10	2824 2937	CAGTGCCCAG [T/C] GGCCG			(:		3 (3)	3' UT	
		TGGTTTTGTT [G/C] CCTGA	CACAG	11	(4	1)	3 (1)	3' UT	
1284.1	249	CTGTCGACGA (T/C) CCCTA	CGCCA	 7	(:	. . 7	4 (
. 6	522	GGGGCAGTGC [G/C] GTCAT	CTCCC		()	•	5 (Silent	
. 7	523	GGGCAGTGCG [G/T] TCATC	TCCCT		(4		4 (Val ->	
.10	608	GCCCTTGGGG (G/T) TTGCA			(:	15	2 (3' UT	- 1110
.20	651 	GGGCTGGGGG [G/A] ATCCC	AGCAG	8	(8	3)	2 (2)	3' UT	
1286.20	5366	GGCCATTGCC [G/A] CAGTC	GCAGC	12	(11	.)	2 (2)	3' UT	
1287.10	864	AGGGATGTTAGACGGAATT[C/G]C	2	(2	!)	4 (3)	3' UT	
1289.15	885	ATCATGTGGA [G/A] GGGCC	AGAGG	13	(9))	2 (1)	3' UT	
.22	1006	GGCATTCCAG (C/G) TGAGA	CACTG :	21	(10)	5 (3' UT	
1290.7	929	CCCTCACCCC [A/G] TCACG	CCTCG	3	(1	.)	2 (2)	3' UT	
1291.5		TCAACAAAAA [G/A] GGACAC								
.8	2168	TAAGTACCAC [G/A] AGCAG	TIGGG	2					Silent	
.12	4517	GCTGACAGAG [G/A] AGGAGG		5		1	2 (1)	Ser ->	rys
.13	5114	CCAGCCTCCA [G/A] TGTACA	ACTT	4	(1	1	2 /	1 1	3' UT	Llys
1292.11	3547	AGGCAAATTC [A/G] ATTTGA	ACAT	7	- 		· 5 (21 Im	
.20	3888	TGTGTGTGTG (T/G)GCTGT	GCTT 1	1	, , , ,				3' UT	
.21	3889	GTGTGTGTGT [G/T] CTGTCG	CTTG 1	.1	9)		3)	3' UT	
	2480	CATGCCTGTG[C/G]GTGCGC								
.11	2481	ATGCCTGTG [C/G] TGCGCT	TCCT	2	(2				3' UT	
						, 	2 (1)	3' UT	
1298.20	960	TTCAGTGGGC[T/C]TTTCTG	GCAG 1	2	ı e	1	2 (٦.١	Tau	Pro
1300.7	566	AAGTGTACCT [T/G] GAATTC	TTTG						N/D	

							·	• • • • • • • • •	
Target	Loc'n	Sequence around	# Varia	1	# Var	a 2	Protein	1	
ID		[polymorphism]	(Lib)		(L1))	Change		
1301.1	2 668	CGCCCGGCTG [G/C] GCA	AGGAGAT	9	(5)				
. 30	1058		ACGCCTC		(7)		3 (1)	Ala ->	
.33	1 1059	AAGGTCTATG [C/G] TGA	CGCCTCC		(6)		3 (2)	Ala -> Ala ->	
									val
1302.7	759		GACCATC	2	(2)		5 (5)	Ser ->	Ala
. 8	806		CAACCCA		(2)		4 (4)	Silent	
.10		an agent (a) ClVII	GCCAAGA	4	(4)		2 (2)	Silent	
. 19			CAGAAGT		(5)		4 (4)	3' UT	
		ACTICIAAAG (C/A) AAG	AGGATAA	8	(7)		9 (9)	3' UT	
1303.5	1226	TGCTGTGCAC [A/G] TTG	actacaa		(5)				
.19	1624	GATTATATAT [T/A] TTT			(5)		2 (2)	Ile ->	Val
. 21	1813	GTGCACTAAT [A/G] TGT.	AAGACAA		(6)		3 (3)	3' UT	
. 22		TTAAATAGCT [C/T] TTT	CTCTGA		(1)	1	4 (8)	3' UT 3' UT	
. 23	2079	TCTATAAACC [A/G] AAC	IGATGTA		(1)		6 (9)	3' UT	
1205 12		***************************************							
1305.12	1434	AATAAACTATAGTAGTGT	r[t/a]t	8	(8)		5 (4)	3' UT	
1306.14	407	TTTGATATTG [C/T] CTC							
.21		TTTTTTTGCA (A/T) AAA	CTAAACT		(2)		4 (4)	Ala ->	Val
			CIAAAI	- Z	(2)		4 (3)	3' UT	
1309.4	466	GCGGGCCGCC[T/C]GCT	TTGGAG	5	(5)		2 (1)	Leu ->	D==
.5	494	AGGAGTATGC [G/A] GCT	CGGCCC		(3)		3 (3)	Silent	PIO
1312.10	492	ACCCCTGGGG [G/A] AGTO	CATCAT	7	(6)		3 (3)	Ser ->	Lys
1315.13		***************************************			-				•
.22		AAGTTCCTCA [C/A] GCCC	TGCTAT		(10)		2 (2)	Thr ->	Lys
		TCCTTTTTTA (A/G) AAAJ	AAAAAA	8	(7)		3 (3)	3' UT	
1317.4	1083	GATAGATTAT [G/A] TATT	CTTCCA		(3)		4 / 3\	*	
				- .			4 (3)	N/D	
1318.2	183	GGGAGCCTGC [C/A] AGGC	TCCGCT	12	(11)		3 (3)	Silent	
1222									
1322.12	876	TGACTCCACA (G/A) CCTC	AGCCGA :	23	(14)	!	5 (5)	Ala ->	Thr
1326.5	139	CCCCCCAAA (c/m) mmaa		- - - ·					
.12		GGCCTGGAAA [C/T] TTGC TAGGAAAGAC [G/A] TCGG	ACAGTC		(5)		3 (1)	Leu ->	
.17		TCCCCAGGGT [T/C] TTCT	CITICG		(2) (2)		3 (3)	Val ->	Ile
.19	2333	ATTCTGAGGG [A/G] TATC	CAGCAG		(4)		5 (3) 4 (2)	Silent	1101
					·		• (2)	Asp ->	Val
1328.5	2968	CCTAAAAGTG [T/G] TTTT	TATTTC	6	(4)	4	(4)	זי טד	
						· 			
1330.13	1526	TTGATCATGA [G/A] ACAT	AGGTAT	6	(3)	:	2 (1)	זט ינ	
1331.15	1666	ACARCACACIC (C) mma							
. 24	2009	ACAAGCACAC [C/G] TTAG CTGCTGATGC [C/T] GTAC	AGGCTT	2 ((2)	10	(4)	3' UT	
					· /)	2	2 (2)	3' UT	
1332.5		AGCTGAACCC [G/C] GAGT					2 (1)	Silent	
1333.4	89	GAGCACAGCG [G/A] CATC	TTTGGC	7 (5)		2 (2)		Asp
.10	279	CCGTGCAGGC [C/A] ATGA	ACCGCA	5 (5)	6	(5)	Ala -> Silent	•
	756		CCTCGC	6 (6)	-	1 (6)	יויון יי	
1335.1	771	3.000000000000000000000000000000000000							
.13	331 872	AGGGCTGGCC[C/T]TTGG	AAGGCG	4 (4)			ידט יכ	
.28					6)		(1)		Phe
			TGAGCG	o (61		(2)	זטינ	
1336.6	851	GCCGCGAGGC [C/G] TGGT	CTGAGC	5 (5)		. (5)	3' UT	
. 7	889	GGTCCTCTCA [G/A] TCTT	CCCCT 2	1 (10)		(2)		
.15	990	GGTCCTCTCA [G/A] TCTT TTGGCAACGG [C/T] CGTC	STCATG 1	7 (11)		(1)	3' UT	
				·		_	,		

Target ID	Loc'n	Sequence around [polymorphism]	# Va	ria ib)	1		ria 2 ib)		otein ange		•
1337.1	2 420	GCAGTCATGC [C/G] GGGTG	ATCGT		32	(15)		3	(2)	3' UT	•
1339.1	7 2972	Tamma om oos (s. /e) ees									
.20			TTTCC			(9)		7	(4)	3' UT	
. 20	3146	GTCGGACAGT [G/T] GCTCA	TAGAG		6	(6)		5	(4)	3' UT	
1741 2											
1341.3	630		rcccc		4	(4)		6	(3)	Silent	;
. 4	633		CCGG		10	(9)		4	(2)	Silent	
.17			CAAA		22	(14)		2 ((1)	Silent	:
. 29			GCCG		13	(8)		2 ((1)	Silent	:
.32	1195	AAACCCAAAA [G/A] GCTCTT	TTCA		7	(5)		5 ((3)	3' עד	
1343 5											
1342.5	142		CGCT	:	11	(9)		3 ((2)	Silent	
.7	227		CAGG		4	(4)		5 (4)	Val ->	
. 8	271		CCCG		11	(11)		4 (2)	Silent	
.10	314	CGCGGCTCGC [G/A] ACAACA	AGAA		8	(8)			2)	Asp ->	
1747 15											
1343.17	514	GAACTCAAAA [G/A] GCTCTT	TTCA		7	(7)		4 (4)	3' UT	
1344.2											
1344.2	149	GAGCGCATCG [C/G]GGGAGA	GGCT		2	(2)		2 (2)	Ala ->	Gly
1345.3	360	000000000000000000000000000000000000000									•
1345.3	360	GGCGCGGTGG [G/C]GTCAAG	CGCA		3	(3)		3 (1)	Gly ->	Ala
1346.1	2260										
.2	2269	CAGACTGGTG [A/G] ACGAAT	ATTC			(2)		2 (2)	Asn ->	Asp
.10	2407		.CCCG			(2)		3 (3)	Met ->	Leu
.10	3265	TGCCGGGCCT [C/T] CCTCCC	GGGG		3	(3)		2 (2)	3' UT	
1347.3	107	Chacocan (a/a)									
.5	107	GAAGCCGAGA [C/G] GGAAAA	TGTC	1		(8)		4 (3)	Arg ->	Gly
.6	111	AGCCGAGACG [G/A] AAAATG	TCAT			(2)		3 (3)	Silent	
.37		CCGAGACGGA (A/G) AATGTC	ATCA			(12)	;	2 (1)	Lys ->	Arg
.38		GGTTCTTGTT [T/G] GGGCAC	AGCA			(11)		3 (3)	זט ינ	
		TTCTTGTTTG [G/T] GCACAG	CACA	1	.7	(11)		4 (4)	3' UT	
1349.4	351	ATCGGGATCG [T/A] GTGTTC									
. 9	1136	GCCCTGCACG [A/G] GCCCAG	CAGT			(1)		9 (•	Val ->	Ser
.10	1137	CCCTGCACG [A/G] GCCCAGG	GGGC			13)		3 (3' UT	
.11	1150	CAGGGGCTGA [G/A] CGTTCC	JGCT			(6)		1 (•	3' UT	
		CACCOCCION (G/N) CGITCC	IAGG	2	0 ((12)	:	2 (2)	3' UT	
1350.4	188	CCAAGCGCTC[T/C]AGGGGC	 								
.5	275	ATGGAAGAGT [T/C] GTGGAA	1116			4)		2 (•	Silent	
.10	473	GGGGCTTTGC [C/T] TTTGTA	CCT			10)		2 (Silent	
.12	770	ATGGATTTGG [C/T] AATGATG	ACCI TONA			8)		3 (Silent	
		TITOURITIES (C) I) ARIGAT	JUAA		5 (5)		2 (2)	Ala ->	Val
1351.25	1695	GTGTGGAGAA [G/A] CCACAGO		1	^ ′	7)		· ·			
						- / /	10) (8)	זט ינ	
1354.23	2233	CAACAATTTT [C/T] TATGTT	ACTT.		7 (
									1)	3' UT	
1355.7	4296	AGCCTTCAGG [C/T] TCGGGGG	GCT		2 (2)				Ala ->	*** 3
.8	4778	GCGCTGATAA (C/G)GTTCATC	AAD			3)	_			3' UT	vai
.10	4785	TAACGTTCAT (G/A) GAACGCO	TTG			5)		. (
							• • • • • • •		1 /	3' UT	
1358.8	2515	CAGGGCGAGT [G/C] GCATGTC	TGC		7 (71		(21	3 (TMP	
.17	2629	CTTGGCATGT [G/A] ATGGCAG	CTC	2	0 (17)			2)	3' UT 3' UT	
					- ·	, 			41	J UI	
1359.3		ATAAATACAA [G/A] AACATTO	GAG		3 (2)	-	- 1	21	C410==	
									. 		
1360.12	548	TGTAAGCTGA (G/C) CCTGGTG	GCC	1	8 (6)	2	1	1)	3' UT	
									-, 		
1361.10	4077	CTGTCTTTCC [A/G] TTTTTTC	ATG	14	4 (9)	2	(1)	זטי 3	
1302.9	1832	CCGCCAGGCG [G/A] ATTTTGT	TCA	:	2 (2)	2	(2)	Silent	

-		•••••••••••••••••••••••••••••••••••••••				-			
Target ID	Loc'n	Sequence around [polymorphism]	# Varia (Lib)		# Variation (Lib)		Protein Change		
.11	2248	CCTATCGGCT [C/G] TTTGCA	GTGG	3	(2)		3 (3)	Leu ->	Val
1363.22	2874	CCGGAATCCA [A/C] AGTGCT	CTGC	2	(2)		7 (5)	3' UT	
1366.3	615			7	(7)	• • • • •	2 (2)	Asp ->	Asn
. 6	722	TGTACAACTT [T/C] CCCGCAC	GGCG	2	(2)		8 (7)	Silent	
1367.18	1851	AAAAAGTAATTCCTTAAA [C/J	A) AT	4	(4)		4 (3)	3' UT	
1368.5	2964	TCTGAGACAC [G/A] CCCCAAC	CATG	3	(3)		2 (2)	3' UT	
1372.1	276	AGATGCTAAG [A/G] TTACCTT	TCC	4	(3)		2 (2)	Ile ->	Val
1373.13	3855	AATATAATAT [C/T] GACACAC	GTGC	4	(4)		 2 (2)	3' UT	
1378.12	4157	TGCTGGGGCA[T/C]GGCGGG	TCC		(2)		-	3' UT	
1383.14	1832	ATCACCACCA [C/T] GTGAGTO	·						
				12	(6)		4 (3) - 	Silent	
1385.17	3454	CAGTGCTAAT [G/A] TGTGCAF	AGCA	7	(5)		4 (3)	3' UT	
1386.31	470	GGGTGACGGG [C/G] CCATGGG	GCG	5	(5)		3 (3)	3' UT	
1387.5	1385			2	(2)	:	2 (2)	3' UT	
.7	1678			3	(3)	!	5 (3)	3' UT	
.8	1900				(4)	:	2 (2)	3' UT	
.11					(13)		2 (2)	3' UT	
.13					(14)		3 (3)	3' UT	
.22					(15) (10)		2 (2) 5 (4)	3' UT 3' UT	
								3. 01	
1388.17	2799	CACAGAAGCA [G/C] CTAAACC	AAG	15	(11)		4 (1)	3' UT	
1395.4	327	CAATGTGTTA [T/C] GTAGTGC	 тта	 35	(17)		 2 (1)	3' UT	
								3. 01	
1396.10	1887	GGCACGAGCC [C/T] TCCTTCT	ATA	3	(3)	:	3 (1)	3' UT	
.12		CCCCAGTGGG [G/A] ACTGAGT	TAT	3	(3)	ţ	5 (2)	3' UT	
.21				2	(2)	;	3 (3)	3' UT	
. 26	2579	AAAGGCTGAA [T/A] TGTCTGA	AAA	10	(7)		3 (1)	3' UT	
1397.23	6232	TATTCAGAGT [G/T] GGCTGGG	ccc		(3)		2 (2)	3' UT	
							· · · · · · · · · · · · · · · · · · ·		
1399.2	177				(3)	:	2 (2)	<- qeA	Asn
	1136	,,,			(3)		(4)	Silent	
.16	1279	CTGCTGTAAA (G/A) GCTGCAG	CCT	8	(8)		2 (2)	זט ינ	
1401.3	71	CCAAGAATCT [G/A] CTGCGCA	TGA	2	(2)		3 (3)	Silent	
.17	874	CCAAGAATCT [G/A] CTGCGCA TTATGTTTAT [G/A] TTTATTA	TGT	8	(6)		5 (4)	3' UT	
.19	917	TTGGAATCAA [G/A] TGTCATA	AGA	8	(7)		5 (4)	3 UT	
.21	1081	TCTACTTTCA [A/C] AAAAAAA			(2)		7 (6)	3' UT	
.23			AAA				3 (3)	3' UT	
1404.12	3921	TGTTGCACAC [T/C] AGCCTTA	 CAG	 3	(3)		2 (2)	3' UT	
1405.15		GTCCACATGC (A/G) CTGGGCG							
								3' UT	
1406.5	4618	TGCTTTCTAG [G/C] TCAGTCC	CTG	5	(3)	6	5 (4)	3' UT	
1407.5		CCCAGGGGGG [G/C] AGCTCCC	TTA	5	(4)			Ser ->	Gln
. 9	713		TGG	10	(7)	2	2 (2) 2 (1)	Silent	

			·						
Target ID	Loc'n	Sequence around [polymorphism]	# Varia (Lib)	1	# Varia (Lib)		Protein Change		
.1	8 1053	GGGCAGGGAA [T/C] CCTGGA	AGCAC	21	(13)				•
. 2	1 1144	GTGGGGTGGG [G/A] TGAGTA	GGAC		(2)		(2) (14)	3' UT	
					· ~/		, (14)	3' UT	
1411.4	2009	GGCGTCAGAG [A/G] TGCTGG	GTGA		(4)	7	(5)	3' UT	
1414.1	3 930	ACATACGAAC [C/T] GCCTCC			(13)	3	(2)	3' UT	•
1415.24	4 1362	GTGCGATTCT [A/G] GATAAR	ייבביי		(5)				
. 20					• - •		(3)	N/D	
				10	(8)	3	(3)	N/D	
1420.6	461	CAGCGGGAGC [G/T] TGAAGA	AAGA	2	(2)		(2)		•
. 8	685				(8)		(2)	Arg ->	
. 9	689		GCCA		(12)		(2)	Val -> Silent	
.10	853		TCTA		(19)		(2)		
								Val ->	rea
1421.8	169	AAGTATACAG [A/G] ACAGAT	TACA	20	(14)	2	(1)	Silent	
. 25	1166		TGCC		(3)		(2)	3' UT	
. 26	1167		GGCC		(3)		(7)	3' UT	
.29	1275		CTTA		(5)		(11)	3' UT	
	• • • • • • • •								
1422.7	278	CCGGGAACCG [G/C] CCACCA	TCAA	4	(3)	3	(3)	Ala ->	Pro
1424.3	1012	GGGAGGATGC [T/G] CTCTCT	cgcg	2	(2)	5	(3)	Silent	
. 4	1021				(3)		(1)	Silent	
. 7	1295		GAAA		(2)		(2)	Trp ->	
	·								λιg
1425.3	274	GCACTGGAGG [G/T] TTTAAT	TTTG	2	(2)	2	(2)	Gly ->	Val
1426.2	1364	GATCACCAGA [T/C] ACCAGG	GTGT		(6)				
.17		TCTCCAGAGT [C/T] ACTCCG			(4)		(1) (3)	Tyr -> Ser ->	
							. 3/	Ser ->	Leu
1427.3	90	CGCCGGCTGC [G/C] CTGCAG	GTGA	8	(6)	3	(1)	Silent	
. 4	91	GCCGGCTGCG [C/G] TGCAGG	TGAC		(6)		(1)	Leu ->	
. 6	109	GACAGTTCGT [G/A] ATGCTA	TAAA	12	(6)		(2)	Asp ->	
.11		TCTTCAGGGG [A/G] CCCAAT	GGTG	7	(2)		(2)	Glu ->	
. 23	-	CTATTCATAA (A/C) GGAAAA	CGAT	10	(5)	12	(7)	3' UT	
. 24		TAAAGGAAAA [C/T] GATTTC	TAAA	21	(10)	2	(2)	3' UT	
.31	_	CAAATTATAT [C/A] ACATTT		8	(3)	13	(10)	דטינ	
.34	-	GCAGAGTCCT [G/C] ATGAAA	GATG	13	(7)	5	(4)	3' UT	
.37	1433	GCATATAATA [C/T] ACATTT	ACTG	6	(2)	9	(7)	3' UT	
1430.3	682	TCTTTGGGGA [G/A] TCAGAT	GAGC	7	(6)	2	(2)	Ser ->	Glu
1431.2	79	GCCAGTGGCG [C/T] TTCGTC	BACG		 /			0:3	
. 6	296	- • - • - •			(6) (7)		(2)	Silent	_
					· //	. '	(6)	Ala ->	Pro
1432.8	2640	AAGTTGCTTA [G/A] AGAGCC	ACCA		(7)		(1)	3' UT	
. 9	2695				(9)		(3)	3' UT	
								3 01	
1433.7	1695	AGCCGGGCTG [C/T] TACCTG			(3)	2	(2)	Silent	
.10	2052	CCCCTGGGTG [C/T] GGGGTG	ATCG		(2)		(2)	Silent	
.11	2160	ATGAGTCCAC [T/C] CTGGCC	TTCC		(2)		(2)	Silent	
. 23	2698	GGACCTTCGA [G/A] GGCCTC	rgcc		(4)		(3)	3' UT	
.28	2787	GTGGAGGAGA [G/A] GCCTGT	GCC		(6)		(2)	3' UT	
.30	2844	GGTGGCGCAG [C/G] CTTGGT			(13)		(6)	3' UT	
.31	2848	GCGCAGCCTT [G/A] GTAACG			(13)		(6)	3 UT	
.32	2857	TGGTAACGCC [A/G] TGGACTO			(14)		(6)	3' UT	
.33	2877	GCGACAATCA [A/G] TGGATGO			(14)		(6)	3' UT	
.34	2942	CCCTACCTGT [C/T] TTATTT			(14)		(9)	3' UT	
							· - /		
1434.15	2041	ACTGTACCTT [C/T] TATGGTT	TTGC	2	(1)	5	(4)	3' UT	

						. -			
Target ID	Loc'n	Sequence around [polymorphism]	# Varia (Lib)	1	Waris (Lib)		Protein Change		•
.1	7 2127	TGATTAGAAC [G/T] GGTAGCC	acr		/				
.10	8 2154		מממ		(1)		5 (4)	3' UT	
			~~~ 	- <b>-</b> -	( 1)		5 (4)	3' UT	
1437.10	2829	AGTTTAAGAT [G/C] ACTTGAC	ccc	5	(4)	••••	 2 / 2\		'
.19	3129	CATGCGTAGC [C/T] TCTTGTC	TTA		(5)		3 (2) 3 (2)	יטינ זטינ	
							J ( Z)	3.01	
1440.5	940		TTG	2	(1)		3 (3)	Silent	
. 6	1327		CGC	2	(1)		2 (2)	Silent	
. 9	1906	- Contract (C) 1 Contract (C)	ATA	2	(1)		2 ( 2)	Ala ->	
.14	2282	TCTTAGAGGC [C/T] TTTCTTG	TAT	2	(2)		3 (3)	3' UT	
1443.4	1042	Composed to the second							
1443.4	1943	CTTCGTGCGA [G/A] AACCTGA	GAA	3	(2)		2 ( 1)	Glu ->	Lys
1444.31	1905	CCAACAGCCT [C/T] CAAAGATO							
		CCAACAGCT [C/T] CAAAGAT(	<del>J</del> GG	3	(2)	2	8 (20)	3' UT	
1445.4	425	CCAGGCTTGC [C/A] AGCCGAA							
.25	1281		100		(5) (4)		2 ( 2)	Pro ->	Gln
			···		(4)	'	4 (4)	3' UT	
1446.3	1227	AGGTGTGGAA [C/T] ACCCTCAC	CG	2	(1)		2 ( 2)	0/1	
.17	3090	TTATTTATAT [T/C] TTTAACAT	'AA		(7)		2 ( 2)	Silent 3' UT	
							• ( 2, •••••	3. 01	
1447.8	2681	GGCAATAGCA [A/G] TCTTGGCT	rga.	3	(3)		3 (2)	זיטי צ	
							·	· <b></b>	
1448.2	521	AGAAGACCAC [A/G] ATGCGAGA	NTG	3	(2)		3 (1)	Silent	
.3	587	GTCATGCTCT [T/C] GCACTTT	<b>ICA</b>	4	(3)		3 (1)	Silent	
1449.20	1261	TCCCTA A DCCC (a / a ) c c c c c c							
.28		TGCGTAATGC [G/A] GCCGAAGA CTGAGAGCCC [C/G] AGGCGTCC			(3)		L (13)	Silent	
.31		TTGCAGATTG [A/C] ATAAAAA	GC :		(14)		2 ( 1)	3' UT	
.32		TGCAGATTG [A/T] TAAAAAA			(6)	6	,	3' UT	
.33		GCAGATTGAA [T/A] AAAAAAAA	AA :		(7)		3 (3)	זט ינ	
		MANAMA (1/1)	MA.	ь	(6)	4	(4)	זט ינ	
1450.2	156	CCCCATGGCG [G/A] CCGCCAAG	GA :		(9)				
				·	·		2 ( 2)	Ala ->	Tnr
1451.13	200	GATGAGCGTG [A/T] TTCCTCTC	GA.	3	(2)	3.1	. (20)	Asp ->	Va 1
.14	. –	ATGAGCGTGA [T/A] TCCTCTCG	AT		(2)		(20)	Asp ->	
.18	417	AAGTTCACAT [C/G] AACCTCAT	GG		(1)		(18)	3 UT	Olu
				- <b>-</b> -	·				
1452.12		GTACCAGAGG [C/T] ATGCCTAT	CA	4	(4)	2	(1)	Ala ->	Val
.18		ATTTAAGGAC [G/A] AGACCAGC	AG	3	(3)	9	(5)	Silent	
.19 .23		CGAGACCAGC (A/G) GCTAATCC	AA	9	(8)	3	(1)	Silent	
.23	2717	GTTAATGATG [T/A] TAATGATT	TT 1	.7	(13)	5	(3)	3' UT	
1454.3	338	ACCCTTTCC (C/T) TTCCTTCA							
.7		AGGGCTTTGC [C/T] TTCGTTCA CATGCTCACT [G/T] TTCTCCCC			2)		(2)	Silent	
. 8	1391	GTTTTAAAAAA [A/T] AAAAA			( 6) ( 2)		(1)	3' UT	
							(3)	3' UT	
1455.6	294	CCAGGCCTTT [G/T] TCATCTTC	AA	9 (	A)	2	(2)	Val ->	Dho
.22	911	CAGCTCGCGA [T/A] GCCCTGCA	GG 1	3 (	12)		(3)		
.23	912	AGCTCGCGAT (G/T) CCCTGCAG	GG		8)			Ala ->	
							· -/		
1460.1	-		CC	5 (	5)	3	(3)	5' UT	
.30			TC 2	5 (	17)	5	(3)	3' UT	
	154		<b></b>						
1461.5	1452	TCCCCGGGGG [G/C] CTTTGGAT	CG	8 (	7)		(2)	Silent	
.34	1403	GTGTTACTGC [A/G] TTTTGTAC	AA 1	4 (	8)	11	(8)	3' עד	
1463.3	761	CAGCGTGGGG [G/T] TGGCCACT							
	_	CAGCGTGGGG (G/T) TGGCCACTC					(2)	3' UT	
1464.3	21	GCCTGCAGGC [C/T] TCCCGAGG	AG					C()	
				J (	۱ د	2	(2)	Silent	

.ergec	Loc'n	Sequence around	# Varia 1		# Varia	2 P	otein		
ID		[polymorphism]	(Lib)		(Lib)		ange		
.4					(1)		(7)	Lys ->	Ser
. 5	13:	AGACTTATAA [G/A] GTTG	ACCTTA	3	(1)	10	(7)	Silent	
1465.4	89	7 ACTTOCA COO ( m / a) a ca		<del>-</del> -					
.5					(2)		(3)	Silent	
.1					(4)		(2)	Silent	
.3					(8)		(3)	Silent	
.3					(17)		(6)	Tyr ->	Phe
.3					(15)		(9)	Silent	
.3					(20)		(6)	Val ->	Ile
.4					(20)		(5)	Silent	
. 4					(20)		(5)	3' UT	
. 4					(20)		(7)	מטינ	
		GATIGGCACC [17C] AGIG		4	(20)	7	(6)	דטינ	
1467.9	229	CATGGAGGCA [G/A] CCAG	CCCCT	<u></u>	 /				_
	1 235				(4)		(2)	Ser ->	
			.010000			2	(2)	Tyr ->	His
1471.4	304:	CACCCAACCT [G/A] TCCT	тастса	2	(2)		/ 1)		
						. <b></b> .	(1)	3' UT	
1473.9	39	GAAAAGCTGC (C/T) ATTO	TCAAGG 1	 1	(11)	5	(3)	Silent	
.1					(B)		(3)	Silent	
					· •,			Sifeur	
1474.1		TCT [G/A] AACGGAGAGCG	TAGTGA 1	3	(10)	4	(3)	יט י 5	
. 2		CT [A/T] ACGGAGAGCGTA			(11)		(3)	יטי כ	
. 9					(14)		(1)	Ser ->	••
. 2	4 37				(15)		(2)	Leu ->	
. 2	6 39:				(14)		(1)	3' UT	F 110
		• • • • • • • • • • • • • • • • • • • •			·,				
1476.6	23	CACAAGTGCC [C/T] TTC	GAGCAGA 1	2	(9)	2	(2)	Silent	
· <b></b>									
1477.2	0 147	ATTTGATGGA [G/C] GCTG	CCCCCGG 3	1	(12)	6	(4)	Ser ->	Ast
. 2	4 148	GGCTGCGCCG[G/C]AGTC	SAAGAGG 3	4	(14)	2	(2)	Ser ->	
.2	8 164	7 TTCCTGTTGA [A/T] AAAA	LAAAAAA	9	(6)	3	(2)	זט ינ	
1478.1				7	(11)	2	(2)	Ala ->	Th:
. 2				6	(18)	2	(1)	3' UT	
. 3	0 109	5 AATAAACTCTTAAAGA[G/	A] CCTT	2	(2)	24	(16)	3' UT	
1480.1					(13)	2	(2)	Val ->	Le
.1					(13)		(2)	Silent	
.1					(12)	4	(4)	Silent	
.2					(10)	4	(4)	Arg ->	Pr
. 2	9 1111	TAGGCATGCC [G/C] CCTC	CCGGGAA 2	0	(13)	2	(2)	Silent	
1403 1						<b>-</b> -			
1483.1					(1)		(2)	Silent	
1484.2									
	14	ATTACGATGA [G/A] GAGO	GAAGAGC	3	(2)	12	(8)	Ser ->	Gl
	20	o CIGIGGCIIG [G/A] AGCA	ATCUTTU	8	(7)	2	(2)	Ser ->	Lv
	- 67	AGCACTTTGT (G/C) CTGC	SACGAGT	3	(3)	2	(2)	Silent	
1496 2	4 643	7							
		GCATTAACTA (A/T) AAAA				7	(5)	3' UI	
1487.1		6 66666336661613366							
	0 220	GCGCCAAGCC (C/A) AGCA	AGGCTAC		(3)			Pro ->	
.2	.u 330.	AGCCACGGGC [G/T] TCCT CTGGGGAAGC [T/C] CCTC	TACTGAG	В	(7)	3	(3)	Val -> Leu ->	Ph
.2						2	(2)	Leu ->	Pr
		2 ACTCNACTON (G (A) COM							
1489.1		9 ACTCAACTCA (C/A) GGTA					(3)	3' UT	
1490.6									
		AGGCTGCTCG [T/C]GTTC CTCGTGATGC [A/G]TCTA			(2)	2	(2)	Val -> 3' UT	Al
					1 7 1				

	- <b></b>		. <b></b>				
10		Sequence around [polymorphism]	# Varia (Lib)	1	# Varia	2 Protein	
.3	3 1824	GTGGGGGTAC [C/T] ATC	TCAACTG	7	(4)	13 ( 9)	3' UT
1491.2	1 1488	GCATATGGGA (G/C) CC	TTCCCTC	11	/ 0\	·	
- 3	1 1826	GCATATGGGA [G/C] CC: TGTAAGGTTT [C/T] CAT	1: 100C10	11	(8)	2 ( 2)	Ser -> Asp
		· · · · · · · · · · · · · · · · · · ·	ITIAGITI	28		3 (1)	3' UT
1495.3		CAAAAACCCC [G/A] CCC	CCTCCAA	3	(2)	3 (2)	Silent
1496.5	301						
.1			CTTTTCA		(4)	2 ( 2)	3' UT
					(1)	•	3' UT
1497.1							
.1.			GGTGGGC		(2)	5 (5)	Silent
.1					(2)	5 (5)	Val -> Ala
. 2			CAGCGAG		(4)	2 (2)	Ala -> Val
.2					(4)	5 (3)	Silent
					(3)	3 (2)	Silent
. 3				3	(2)	6 (5)	זט ינ
. 4			rgggaacc	12	(10)	2 (1)	3' UT
. 4	4 4254	==================================	TTTTTAAA	2	(2)	11 ( 9)	3' UT
1498.5		GGCGTGCTGA(G/C)TG	CCTGGGA	8	(4)	3 (3)	Ser -> Thr
1500.1	6 2206	GAAGGAAACA [G/A] TG	TABCAGCA	16	(13)		
. 1		GTTGTTAAGA [G/T] TGG	CCCACAC		(18)	2 ( 2)	3' UT
. 2	3 2426				(7)	2 (1)	3' UT
		TOCOMOCIO (G/R/RCC	CACGAG	10	( /)	4 (4)	3' UT
1501.5		GCGCTGTGCG (G/T) TG	receera		/ 3\		
	6 123	CCCCGGAGG[G/1]1G	TCACTCA	2	( 2)	2 ( 2)	Silent
		CCCCGGGAGG [G/A] AG	LIGACIGA	•	( 8)	2 (2)	זטינ
1505.9	3934	TTAGTCATTC [T/C] AA	AAACACC	6	(4)	4 ( 4)	3' UT
1507.2	130	CCCCGAGGCG[A/T]TCC	STGGAGGA	3	(3)	3 ( 2)	Ile -> Phe
1508.1	9 511:		regecce	12	(10)	3 ( 2)	N/D
1510.6	1066						
	1136	CAAAGGAGCT [T/C] GAJ TCTAAAAGAA [A/G] AAG	CANCERC	2	( 2)	5 ( 5)	3' UT
		TCIAAAAGAA (A/G) AAC	GGAACTAG	3	(2)	2 (1)	3' UT
1511.1	0 22		AGGAGTC	18	(11)	2 ( 1)	Gln -> Glu
1514.6	103	CGGGGCTGCG [G/A] CCC	CCCCACC	11	/ = \	4 / 4	
. 2					(5)	4 (4)	5' UT
.3					(5)	6 (5)	3' UT
.3					(12) (11)	2 (1)	3' UT
. 3					(11)	3 (2)	3' UT
. 4	3 1069	AGACCCCAGG [G/T] CAC	CATCTCG	21	(9)	3 ( 3) 5 ( 4)	3' UT
1515.6	175	CATGCTAGCA[T/G]GGG	CTAATGA				Trp -> Gly
	8 859	CTGGAGAGCT[T/G]GG			(11)	4 (4)	Silent
		GAGAGCTTGG [C/G] TT		6	(6)	7 (5)	Ala -> Gly
	8 1146		CATTTGCA	2	(2)	23 (14)	3' UT
1517 -							
1517.9	743	AATCATAATG (G/C) TT	TCCCCTT	6	(3)	2 ( 2) 3 ( 3)	Val -> Ala
.1	6 1424	AAGTTATTGG [C/T] AAJ	ACGAGGTT	11	(7)	3 (3)	Ala -> Val
			· <b></b>				
1518.8	94	AGAGCTGAGC [G/A] AG	TTCACCAC	5	(4)	2 (2)	Ser -> Lys
1519.1		CCATCAAAAG (C/T) TT	· <b></b>			6 ( 5)	Silent
						·	
1520.1	2 6696	CAGCCTCATC [G/A] ATO	CCAAAAC		(2)		Asp -> Asn
.1	3 680	TGCGCGGGAG [C/A] AA	ACTGCTCT	2	(1)	3 (1)	Ser -> Arg

Target ID	Loc'n	Sequence around [polymorphism]		ria 1 ib)	#	Varia 2 (Lib)		tein nge		
1521.6	853	AGACTCTGAG [G/C] (	·			·				_
.1						6)		2)	Arg ->	Ser
.1								1)	3' UT	
.1								1)	3' UT	
		CANACIGIG (C/A)	MIIGIGIGC	,	,	4)	) د	1)	3' UT	
1523.7	41	CACCACGGTG[C/T]	GGAATTGTT	9	(	8)	3 (	3)	Silent	
1524.1	3 2996	AAAATGACAT[T/G]	GTTTGAAAA	3		2)	3 /	(2)	3' UT	
. 2				-		9)		(4)		
. 2						7)		(5)	3' UT	
. 2						1)		(3)	3' UT	
.2				25				(2)	3' UT	
							، د	. 21	3' UT	
1526.6	2476	TGGAGGTGCA[T/C];	ACCTACTTA	2	1	1)	2 2	1)		
.7						2)			Silent	
					· .	_,	، د	1)	<pre>Asp -&gt;</pre>	ATA
1528.6	770	CCAAAAGGAA [G/A] 1	GARTCAGCA	2	1	2)	2	(2)		
.1						1)		(4)	Val -> Val ->	
. 2					-	B)		(6)		
.3				19					Asp ->	HIS
							2	(1)	3' UT	
1530.8	42	ATCCGCCCC [A/G]	CACCTCCC	1		3)			mb	
.1						5)		(1)	Thr ->	
.3						3)		(6)	Ser ->	GIU
	·		occonsocc			31	_ , 1	6 6)	זט ינ	
1532.6	496	TCGTGCGCAA[C/T]	TGCCCTGG	4	,	2)	6	(3)		
.1		,-,-,-,-,-,-,-,-,-,-,-,-,-,-,-,-,				4)		(2)	Silent Cys ->	<b>5</b> 4.
					· ·	•	2	( 2)	Cys ->	Pne
1533.1			CACACAGGAA		(	3)		(2)	Asp ->	Ala
1534.4	264		TTCACCATC		( 	1)		(4)	Silent	
1536.2	2 664	TTAGATATAT [A/G]	רבידרבידרים	3	1	3)	4	( 3 )	זטינ	
. 2						2)	11		דטינ	
. 2						3)	4		3 UT	
					· ·					
1537.5	87	AGGGCAGTGC [C/A]	ATTGATAGGA	7	1	6)	3	(3)	Silent	
.1	0 146					7)	3		3' UT	
1538.2	93	CCTCCACCTT[T/C]	BACGCTGGGG	14	(	7)	3	(2)	Silent	
1539.1	6	7 TCGCGGCCTA[G/C]	TTTACCCGC	3	{	3)	2	(1)	יט כ	
. 3	30				i	4)		(3)	Silent	
. 9	107	GTAGCGCCAG[A/C]	CTACGCATTC			2)		(2)	Arg ->	Ser
.1	6 204			8	(	7)		(2)	דט ינ	
. 2	1 271	GCCTAACATAA [A/G	AAAAAAAA							
1541.1	412	3 TGGCGAGGGG [G/C]	CTTGACGGCG	2	(				3' UT	
1543.4	31	GCACCGGAAG [G/A]	AGGCGCTGAC	6	( 	5)	2	(2)	Ser ->	Lys
1544.3		TTGAGCCCAA[C/G]							Asn ->	Lva
		ACTGCTTGGA[C/T]			i	4)	7	(4)	Silent	-10
. 8	64	ACCTGTGTTC[T/A]	CAAAGATGGC	12					Ser ->	
.1	.2 72	8 GCTGCCCAGG [C/G]	TGTGCAGCGC	12	è	11)		(1)		****
.2	1 90	2 AACATCCCCT [C/T]	CATCATTAC	5			4			
. 2	2 98	6 CTGCCTGGCC[C/T]	CTCGCCTGTG	5	ì	4)			3' UT	
1545.4	147	O CGGTGAGACC[G/A]		2	(	1)	2	(2)	Val ->	
1546.1	17	2 CTCTGAAGAC[A/T]					3			

_								
Target ID	Loc'n	Sequence around [polymorphism]	# Varia (Lib)	1	# Varia (Lib)	2 Protein Change		
1547.17	7 976	TGCTTTAAAG [G/A] GCC	GCCTGG	13	(10)	2 ( 2)	3' UT	
1548.3	1209	CATTATTGGC [C/T] TCAT	CAAACC	3	(3)	3 ( 1)	Leu ->	Dhe
. 4	1286				(2)	3 (2)	Silent	File
.8	1904				(3)	5 (3)	3' UT	
				- <b></b> -				
1550.7	797	TGGACGCCTT[T/C]CCA	ATCTGA	2	( 2)	5 (2)	Silent	
1551.12	2 2215	CGAGACCATC [T/C] TGG	CCCTCC		(1)	10 ( 9)	3' UT	
.14	2242			_	(1)	9 (8)	3 UI	
.19	5 2341				(1)	9 (8)	3, fl.	
.16	5 2372	GGAGGGAGGG [T/A] CAGG	GGGAGG	3	(1)	9 (8)	3' UT	
1554.13					(5)	2 ( 1)	Ile ->	Met
.14	•				(6)	2 (1)	Silent	
		ATCTGGCTGC[T/C]GAT	ITGCTAT	5	(4)	5 (4)	3' UT	
1555.5	424	TATGGATGCC (A/G) AGC	CCACAA	17	(8)	2 / 1)		0
. 9	519				(7)	3 ( 1) 3 ( 3)	Lys -> Ser ->	
.30					(2)	8 (5)	Ser ->	inr
						·		
1556.7	2031	TGATCTTTGC (C/T) CCT	GTATGC	5	(5)	5 (3)	3' UT	
1560.7	2339	GCATTCAAGA (C/T) GGA	TACAGAG	5	(5)	2 ( 1)	Thr ->	Met
1561.1	9(	CECECOTO CON CONT.						
.5					(2)	2 ( 2)	Silent	
.2					(1) (7)	2 ( 2)	Met ->	Val
.2:					(6)	4 (4)	3' UT	
					·	· · · · · · · · · · · · · · · · · · ·		
1562.1	4 540			21	(9)	2 (1)	Silent	
.3	0 799	AGCCATGAGT [G/T] GGG	TGGGCC	14	(7)	3 (3)	Gly ->	Trp
								•
1563.1	0 3076	ACTCCCCTTC [A/G] TGA	AACCAGA	2 	(1)	2 (2)	Met ->	Val
1564.7	339	CTTTGGAAAG (T/C) GTG	AAAGCTG	15	(10)	2 (1)	Silent	
1566.2	5:	GCAGGCACAG[T/C]GTC			(1)	2 ( 2)	5' UT	
. 4					(1)	4 (4)	Arg ->	uic
.1	0 79:				(1)	4 (4)	Silent	1113
. 2	3 174				(2)	3 (2)	Cvs ->	Ser
.2	4 174:	GCACTCTGTG (C/G) TCC	GCCCAAG	3	(2)	3 (2)	Cys ->	
1567.2	108	GGAATACTGG (G/A) AGA	 ATCTTC:		(3)	2 ( 1)		*
		· · · · · · · · · · · · · · · · · · ·			· + ·		Ser ->	гуя
1571.4	148	AGAGAAAATT [G/A] GGG	AAAAGGT	4	(4)	3 (2)	3' UT	
.1	4 208	7 TCTGTCTGGT [G/A] TGG	TATGAAT		(5)	4 (2)	3' UT	
1576.1				3	(2)	2 (2)	3' UT	
.1					(2)	2 (2)	3' UT	
1677.1								
1577.1					(2)	6 (5)	Asn ->	Asp
.3					(2)	5 (4)	3' UT	
.3					(13)	4 (3)	3'UT	
.4		• • • • • • • • • • • • • • • • • • • •			(14) (6)	4 (3) 3 (3)	3' UT 3' UT	
.5					(5)	5 ( 5)	3' UT	
1578.5	17	TACTTCGACC [G/A] CAA	AAGACGA	7	(7)	2 (2)	Arg ->	His
.1	2 45				(6)	3 (2)	Pro ->	

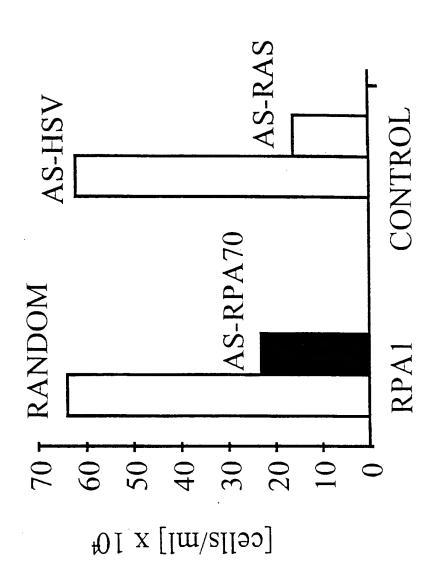
_	roc, r	-	# Varia	1	# Varia	2 Protein		
ID		(polymorphism)	(Lib)		(Lib)	Change		
.1					(6)	3 (2)	Silent	
.1					(5)	2 ( 2)	Val -> 1	Leu
.1					(5)	4 (3)	3' UT	
. 2					(7)	2 ( 2)	3' UT	
. 2					(5)	2 (2)	3' UT	
						3 ( 3/	3' UT	
1579.1	5 173	GCTGCAGCGG [C/T]TGG	CAGACGG	17	(12)	2 (2)	Silent	
.1	9 188	GGATCCGAGA (G/A) GGC	ATGGCCG	14	(12)	5 ( 5)	Ser -> (	Glu
. 2	6 201	O GAATACTCCC [G/C]GCC	AGGGCCT	12	(10)	17 (10)	3' UT	
1581.2					(3)	5 (4)	Met ->	Ile
. 5	223	2 TGAATGTAAC (T/C)GCT	TTAAGAA	3	(3)	5 (5)	3' UT	
1583.7	148	2 AAGACACAGA (A/T) GGA	cccccx		·			_
.1					(5)	3 (2)	Glu -> .	Asp
						2 ( 2)	3' UT	
1584.1	8 57	6 CGCCCTCACA (G/A) CCT	CCTTCTG	2	(2)	2 ( 2)	Silent	
. 3	4 109	8 ATATGGATGG [C/T]GGT	ACCTTCA		(3)	2 ( 2)	Ala ->	Val
. 4	6 170	8 GAGAAACCCC(C/T)GGG	GACCATG	3	(3)	2 (2)	זטינ	
. 5			AGGCACA	2	(2)	6 ( 6)	זט ינ	
. 5	1 185	7 AGCACAGGCA [C/A] AGA	GGTGCTG	2	(2)	6 (6)	3' UT	
1587.1					(2)	11 (10)	Glu ->	Glr
٠.		6 TCCAGAACCC(C/T)GAC	FITCCCAC	18	(14)	2 ( 2)	Silent	
1588.2	6 195	6 TTGTACACAA [T/C] CTC	ATTTCAT	7	(6)	4 (3)	3' UT	
						- ( 5)		
1590.2	17	2 TGCACGCAGC [C/A] ATG	GCTGACA	6	(3)	2 (2)	Silent	
. 7			TACATGG	В	(4)	2 (2)	Silent	
. 9				4	(2)	2 ( 2)	Silent	
. 3	3 213	9 AGCCGACTCT (G/T)GCC	CTGGCCC	14	(9)	4 (4)	3' UT	
1594.1	.0 173	0 ACCCCAGTGG [G/A] AAC			( = )			
.1					(5) (5)	2 (2) 9 (6)	3' UT 3' UT	
. 1					(5)	9 (6)	3' UT	
1596.3	177	3 TGATGTGGTA [C/T] GTG	CCTCCAC	10	(7)	3 (2)	3' UT	
. 6	184	4 GTATTCACCA [A/C] GCF	TTTTAGG	10	(8)	4 (3)	3' UT	
. 1	.1 189	9 GCATTTACAA [G/A] GCA	CTGCCAA	17	(12)	3 (3)	3' UT	
. 1					(12)	2 (2)	3' UT	
. 1	.6 194	9 AGAGGACCTG [C/T]GGG	CTTAGAT	24	(16)	2 (1)	3' UT	
1598.3	204	2 ATGCCTAAGA (C/A) CA/						
		2 AIGCCIAAGA (C/A) CAA	ACIGCGII		(2)	3 (1)	זטינ	
1603.5	5 59	2 TCTGTGGCAC [T/C] GAT	TATGACCA	2	(2)	2 ( 2)	יט יפ	
. 1		• • • • • • • • • • • • • • • • • • • •			(12)	2 ( 2)		Sex
. 1	18 266				(11)	3 (3)	Silent	
. 2	28 295	3 TTAGAATTTT [C/T] CTA	AATAAAA		(18)	2 (1)	3' UT	
	·		·					
1605.1	14 287	9 AACACGGCCC[T/C]GC	rgtcgctg				Leu ->	Pro
		1 AATTTAAAGT (A/C) TTO			(2)	6 ( 6)	3' UT	
1607.1		4						
		4 CTTTCTCTGG[C/T]CC				2 ( 2)	3' UT	
1608.3					(2)	2 ( 2)	יטינ	
	1 255				(9)		3 UT	
	17 273	• • •			(11)	3 (3)	3' UT	
	1 209				(36)	7(7)	3'UT	
	2 212				(18)	47 (40)	3'UT	
		• • • •			·•		- <b>-</b> -	
. (	04 257	'8 Gaaataaaag [t/g] ag	CCCAGCTG	26	(19)	46 (29)	3'UT	

201 / 214

1611.20		AACACTGGTGCCAACCAA [G/A] AC	3 ( 3)	3 ( 3)	ייוז ו 3
.07		TTTGCAAGGA [A/G] GGCCTAATCA	66 (36)	6 (6)	Silent
.06	2174	CCTCTCCCAG [C/T] GGCCTCCCCC	71 (36)	1(1)	Silent

	• • ·									
Target ID	Loc'n	Sequence around [polymorphism]	#	Varia (Lib)	1	#	Varia 2 (Lib)	Protein Change		
1613.2	350 1 842				10		7) 3)	3 (3) 6 (4)	Val -> 3' UT	Ile
1614.5 .1: .2:	3 2158	CGGCGTGGA [G/A] GCTGA TTTTTTTTT [T/A] AAAAA	.GCG(	CC Aa	10 7	(	2) 9) 7) 5)	3 ( 3) 2 ( 2) 8 ( 5) 2 ( 2)	Silent Ser -> 3' UT 3' UT	Glu
1615.2	5 2113	CCTGGCCATC[T/C]TGGGC	AGT	gt	16	(:	 11)	7 (5)	Silent	

Fig. 9



f19.10

Variance Specific Inhibition of mRNA levels by Oligonucleotides Against RPA1

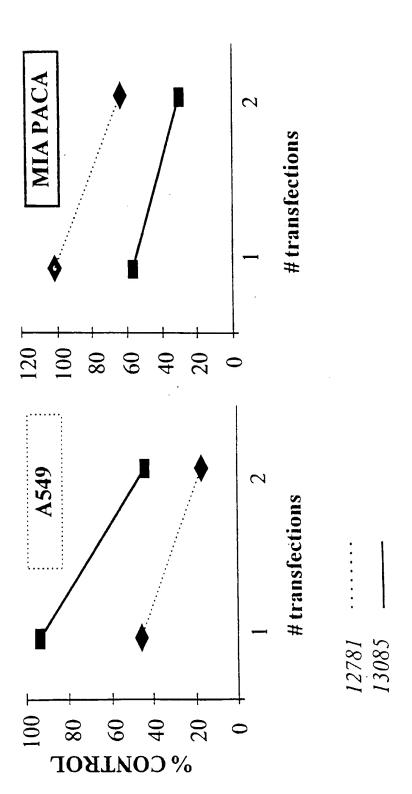
13706 13085 MiaPaca II 12781 13706 13085 T24

oligo cell

	T24 Cells	Mia Paca II Cells
Oligo:	ISIS 13706 ISIS 12781 Varia 13085	ISIS 13706 ISIS 12781 Varia 13085
Northern	match	match
RNA		
DIVA		

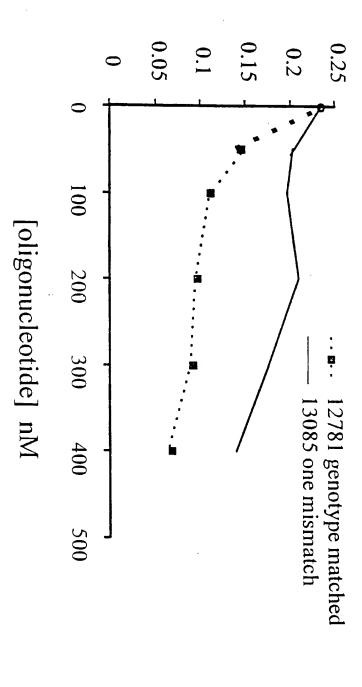
F15, 11





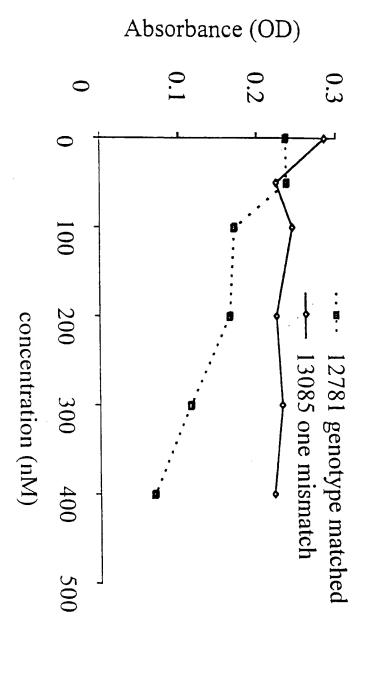
F13.13

BrdU incorporation



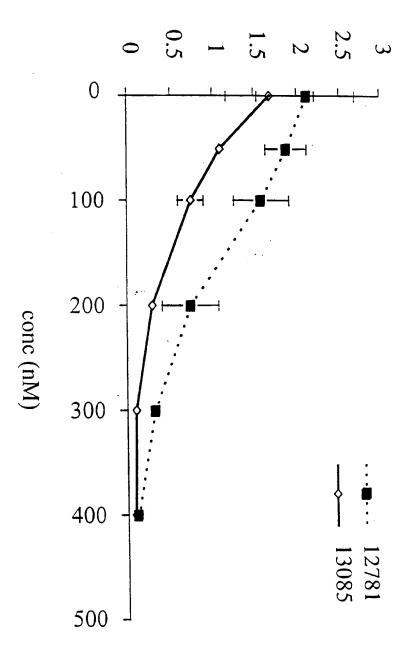
# Proliferation by Oligonucleotides Against RPA1 Variance Specific Inhibition of A549 Cell

F18.14

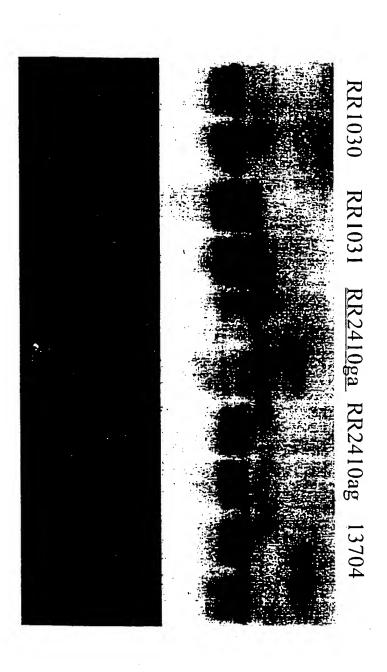


# Variance Specific Cell Killing of A549 Cells by Oligonucleotides Against RPA1

# absorbance



F18.16



Suppression of Ribonucleotide Reductase mRNA

## MDA-MB 468 Cells

13706 2410AG 2410GA

Oligo:

Northern



match

RNA



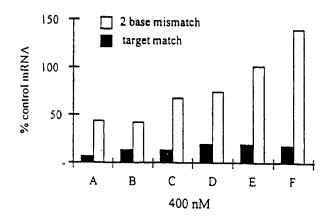
Fig. 17

Fig. 18

# Research Collaboration

A	ACAGCCACTTATGTCATGGT
B	ACAGCCACTTATGTCATGGT
C	<u>ACAGCC</u> ACTTATGT <u>CATGGT</u>
D	CACTTATGTCATGGTATTCA
E	CACTTATGTCATGGTATTCA
F	CACTTATGTCATGGTATTCA

# Improved Allele-Specificity with Advanced Chemistry



Effect of Antisense Oligomers on Glutamylprolyl-tRNA Synthetase (EPRS) mRNA levels (duplicates)

14977 (100% matched)

conc 0 50 100 200 300 400



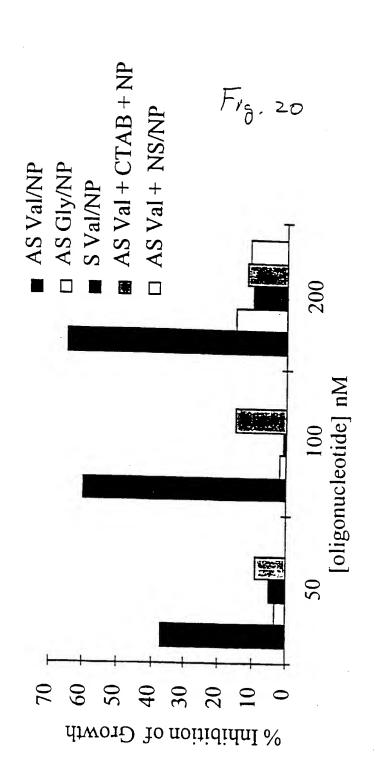
14971 (2 mismatches)

0 50 100 200 300 400 nM

*circled samples were switched when loaded on to the gel

Fig. 19

Example: Allele-Specific Inhibition of Ras



Schwab et al., 1994



### **PCT**

### WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



### INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:
C12Q 1/00, C07K 14/00, A61K 35/00,
C12N 15/00

(11) International Publication Number: WO 98/41648

(43) International Publication Date: 24 September 1998 (24.09.98)

(21) International Application Number: PCT/US98/05419

(22) International Filing Date: 19 March 1998 (19.03.98)

(30) Priority Data: 60/041,057 20 Man

20 March 1997 (20.03.97) US

(71) Applicant (for all designated States except US): VARIAGEN-ICS, INC. [US/US]; One Kendall Square, Building 400, Cambridge, MA 02139-1562 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): HOUSMAN, David [US/US]; 64 Homer Street, Newton, MA 02159 (US). LEDLEY, Fred, D. [US/US]; 433 Grove Street, Needham, MA 02192 (US). STANTON, Vincent, P., Jr. [US/US]; 32 Royal Road, Belmont, MA 02178 (US).

(74) Agents: WARBURG, Richard, J. et al.; Lyon & Lyon LLP, Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071-2066 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

### Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:
29 April 1999 (29.04.99)

(54) Title: TARGET GENES FOR ALLELE-SPECIFIC DRUGS

### (57) Abstract

This disclosure concerns genetic targets which have been found to be useful for allele specific anti-tumor therapy. The strategy for such therapy involves the steps of: (1) identification of alternative alleles of genes coding for proteins essential for cell viability or cell growth and the loss of one of these alleles in cancer cells due to loss of heterozygosity (LOH) and (2) the development of inhibitors with high specificity for the single remaining alternative allele of the essential gene retained by the tumor cell after LOH. Particular categories of appropriate target genes are described, along with specific exemplary genes within those categories and methods of using such target genes.

### FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
ΑT	Austria	FR	France	LU	Luxembourg	SN	Senegal
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
ΑZ	Azerbaijan	GB	United Kingdom	MC	Моласо	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	1L	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of Americ
CA	Canada	IT	Italy	MX	Mexico	UZ.	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		2311102040
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

Internal ial Application No PCT/US 98/05419

4 61 466	FIRST TOWN OF OUR THE THE	PC1/US 98	5/05419		
IPC 6	IFICATION OF SUBJECT MATTER C12Q1/00 C07K14/00 A61K35,	/00 C12N15/00			
1		·	<u>.</u>		
According t	to International Patent Classification (IPC) or to both national classifi-	cation and IPC			
B. FIELDS	SEARCHED				
Minimum di IPC 6	ocumentation searched (classification system followed by classification C120	tion symbols)			
	,				
Documents	tion searched other than minimum documentation to the extent that	such documents are included in the fields so	embed		
		The state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the s	A 51184		
Electronic d	data base consulted during the international search (name of data be	ase and, where practical search terms used			
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT		· · · · · · · · · · · · · · · · · · ·		
Category °	Citation of document, with indication, where appropriate, of the re	levant passages	Relevant to claim No.		
Х	WO 95 03335 A (HOUSMAN DAVID E ;	K 0	1,13,21,		
	TECHNOLOGY INC (US)) 2 February cited in the application	1995	29,37, 38,53,		
	avious in the appropriation		54,69,		
			77-79,		
	see the whole document		101,109		
A	WO 97 04087 A (KRUPP GUIDO ;MARG	ET			
	MATTHIAS (DE): WESTPHAL ECKHARD	(DE);			
	MUELLER) 6 Fébruary 1997				
Α	WO 94 11494 A (UNIV JEFFERSON ;P	ROCKOP			
	DARWIN (US); COLIGE ALAIN (BE); RE) 26 May 1994	BASERGA			
Α	US 5 491 064 A (LICHY JACK H ET	AL) 13			
	February 1996				
		-/			
X Furth	er documents are listed in the continuation of box C.	X Patent family members are listed in	n annex.		
° Special cat	egories of cited documents ;	*T* later document published after the inter	netional filing date		
"A" docume conside	nt defining the general state of the art which is not ered to be of particular relevance	or priority date and not in conflict with t cited to understand the principle or the	he application but		
	ocument but published on or after the international	"X" document of particular relevance; the cl	aimed invention		
'L' documer	nt which may throw doubts on priority claim(s) or s cited to establish the publication date of another	cannot be considered novel or cannot involve an inventive step when the doc	ument is taken alone		
citation	citation or other special reason (as specified)  cannot be considered to involve an inventive step when the				
other m		document is combined with one or mot ments, such combination being obviou in the art.			
later th	an the priority date claimed	"&" document member of the same patent for	amily		
Date of the a	ctual completion of the international search	Date of mailing of the international sear			
9	December 1998	16. 03.	1999		
Name and m	eiling address of the ISA	Authorized officer	-		
	European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,				
	Fax: (+31-70) 340-3016	MOLINA GALAN E.			

Intern. Ial Application No PCT/US 98/05419

Continua :	ition) DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/US 98/05419		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
Р,Х	WO 97 32024 A (TRINITY COLLEGE DUBLIN ;FARRAR GWENYTH JANE (IE); HUMPHRIES PETER) 4 September 1997	1,13,21, 29,37, 38,53, 54,69, 77-79,		
	see the whole document	101,109		

International application No.

PCT/US 98/05419

Boxi	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	emational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  Remark: Although claims 37, 53, 69 and 109 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.	Claims Nos.: because they relate to parts of the international Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of Invention is lacking (Continuation of Item 2 of first sheet)
This Inte	mational Searching Authority found multiple inventions in this international application, as follows:
see	FURTHER INFORMATION sheet
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is estricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1, 13, 21, 29, 37, 38, 53, 54, 69, 77-79, 101 and 109
Remark o	n Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1, 13, 21, 29, 37, 38, 53, 54, 69, 77-79, 101 and 109

Inhibitors (in particular nucleic acids) targeting at least one but less than all alleles of a gene vital for cell growth or viability and encoding a product required for cell proliferation wherein cells not targeted by the inhibitor have at least one alternative variant allele, methods for identifying, producing and using such inhibitors and pharmaceutical compositions comprising them.

2. Claims: 2, 14, 22, 30, 39, 40, 55, 56, 70, 80-82, 102 and 110

Inhibitors (in particular nucleic acids) targeting at least one but less than all alleles of a gene vital for cell growth or viability and encoding a product required to maintain inorganic ions and vitamins at levels compatible with cell growth or survival wherein cells not targeted by the inhibitor have at least one alternative variant allele, methods for identifying, producing and using such inhibitors and pharmaceutical compositions comprising them.

3. Claims: 3, 15, 23, 31, 41, 42, 57, 58, 71, 83-85, 103 and 111

Inhibitors (in particular nucleic acids) targeting at least one but less than all alleles of a gene vital for cell growth or viability and encoding a product required to maintain organic compounds at levels compatible with cell growth or survival wherein cells not targeted by the inhibitor have at least one alternative variant allele, methods for identifying, producing and using such inhibitors and pharmaceutical compositions comprising them.

4. Claims: 4, 16, 24, 32, 43, 44, 59, 60, 72, 86-88, 104 and 112

Inhibitors (in particular nucleic acids) targeting at least one but less than all alleles of a gene vital for cell growth or viability and encoding a product required to maintain cellular proteins at levels compatible with cell growth or survival wherein cells not targeted by the inhibitor have at least one alternative variant allele, methods for identifying, producing and using such inhibitors

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

and pharmaceutical compositions comprising them.

5. Claims: 5, 17, 25, 33, 45, 46, 61, 62, 73, 89-91, 105 and 113

Inhibitors (in particular nucleic acids) targeting at least one but less than all alleles of a gene vital for cell growth or viability and encoding a product required to maintain cellular nucleotides at levels compatible with cell growth or survival wherein cells not targeted by the inhibitor have at least one alternative variant allele, methods for identifying, producing and using such inhibitors and pharmaceutical compositions comprising them.

6. Claims: 6, 18, 26, 34, 47, 48, 63, 64, 74, 92-94, 106 and 114

Inhibitors (in particular nucleic acids) targeting at least one but less than all alleles of a gene vital for cell growth or viability and encoding a product required to maintain the integrity and function of celular and subcellular structures wherein cells not targeted by the inhibitor have at least one alternative variant allele, methods for identifying, producing and using such inhibitors and pharmaceutical compositions comprising them.

7. Claims: 7-10, 19, 27, 35, 49, 50, 65, 66, 75, 95-97 and 107

Inhibitors (in particular nucleic acids) targeting at least one but less than all alleles of a gene vital for cell growth or viability and being located on a high frequency loss of heterozygosity chromosomal arm region, wherein cells not targeted by the inhibitor have at least one alternative variant allele, methods for identifying, producing and using such inhibitors and pharmaceutical compositions comprising them.

8. Claims: 11, 12, 20, 28, 36, 51, 52, 67, 68, 76, 98-100 and 108

Inhibitors (in particular nucleic acids) targeting at least one but less than all alleles of a gene vital for cell growth or viability having at least two sequence variances which occur at frequences such that at least 10% of a population is heteroziguous for that gene and wherein cells not targeted by the inhibitor have at least one alternative variant allele, methods for identifying, producing and using

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

such inhibitors and pharmaceutical compositions comprising them.

### 9. Claims: 115-129

Inhibitors (in particular nucleic acids) targeting at least one but less than all alleles of a gene conditionally vital for cell growth or viability wherein cells not targeted by the inhibitor have at least one alternative variant allele, methods for identifying, producing and using such inhibitors and pharmaceutical compositions comprising them.

### 10. Claims: 131-146

Methods using inhibitors targeting at least one but less than all alleles of a gene vital for cell growth or viability wherein cells not targeted by the inhibitor have at least one alternative variant allele related to transplantation and engraftment.

### 11. Claims: 147-150

Methods for separating a cell from a mixture using allele specific binding compounds targeting at least one but less than all alleles of a gene wherein cells not targeted by the compound have at least one alternative variant allele.

Intormation on patent family members

Interns al Application No
PCT/US 98/05419

	tent document I in search repor	t	Publication date		atent family nember(s)	Publication date
WO	9503335	A	02-02-1995	AU AU CA EP JP US	690131 B 7405994 A 2168096 A 0714410 A 9500650 T 5702890 A	23-04-1998 20-02-1995 02-02-1995 05-06-1996 21-01-1997 30-12-1997
WO	9704087	Α	06-02-1997	AU	6657996 A	18-02-1997
WO	9411494	A	26-05-1994	CA EP JP	2148687 A 0674705 A 8503366 T	26-05-1994 04-10-1995 16-04-1996
US	5491064	Α	13-02-1996	NONE		*************
WO	9732024	Α	04-09-1997	AU CA EP	2223897 A 2248869 A 0894140 A	16-09-1997 04-09-1997 03-02-1999